INTERNATIONAL JOURNAL OF
RADIATION ONCOLOGY • BIOLOGY • PHYSICS
www.redjournal.org

ASTRO's 65th Annual Meeting (October 1-4, 2023)

Late-Breaking Abstracts

LBA 01

Randomized Phase III Trial of Postoperative Radiotherapy with or without Cetuximab for Intermediate-Risk Squamous Cell Carcinoma of the Head and Neck (SCCHN): NRG/RTOG 0920

M. Machtay,[1] P. Torres-Saavedra,[2,3] W.L. Thorstad,[4] P.F. Nguyen-Tan,[5] L.L. Siu,[6] F.C. Holsinger,[7] A.K. El-Naggar,[8] C.H. Chung,[9] J. Dorth,[10] N.Y. Lee,[11] J. Chan,[12] N. Dunlap,[13] V. Bar Ad,[14] W.A. Stokes,[15] A. Chakravarti,[16] D. Sher,[17] S.S.D. Rao,[18] J. Harris,[3] S.S. Yom,[12] and Q.T. Le[19]; *[1]Penn State University -Penn State Cancer Institute, Hershey, PA, [2]The American College of Radiology, Philadelphia, PA, [3]NRG Oncology Statistics and Data Management Center, Philadelphia, PA, [4]Department of Radiation Oncology, Washington University School of Medicine, St. Louis, MO, [5]CHUM (The University of Montreal Hospital Centre), Montreal, QC, Canada, [6]Department of Medical Oncology and Haematology, Princess Margaret Cancer Centre, University of Toronto, Toronto, ON, Canada, [7]Stanford Healthcare, Palo Alto, CA, [8]The University of Texas MD Anderson Cancer Center, Houston, TX, [9]H. Lee Moffitt Cancer Center, Tampa, FL, [10]UH Cleveland Medical Center, Cleveland, OH, [11]Memorial Sloan Kettering Cancer Center, New York, NY, [12]University of California San Francisco, Department of Radiation Oncology, San Francisco, CA, [13]University of Louisville/James Graham Brown Cancer Center, Louisville, KY, [14]Department of Radiation Oncology, Thomas Jefferson University, Philadelphia, PA, [15]Winship Cancer Institute of Emory University, Department of Radiation Oncology, Atlanta, GA, [16]The Ohio State University Comprehensive Cancer Center, Columbus, OH, [17]UT Southwestern / Simmons Cancer Center, Dallas, TX, [18]University of California Davis Comprehensive Cancer Center, Sacramento, CA, [19]Department of Radiation Oncology, Stanford University School of Medicine, Stanford, CA*

Purpose/Objective(s): The combination of radiotherapy (RT)/cetuximab has demonstrated superiority over RT alone for locally advanced non-operative SCCHN. We performed a definitive randomized trial to test this hypothesis in completely resected, intermediate-risk SCCHN.

Materials/Methods: Enrolled patients had SCCHN of the oral cavity, oropharynx or larynx (hypopharynx was excluded); complete resection with negative margins and no evidence of nodal extracapsular spread; but one or more risk factors warranting postoperative RT. Patients were randomized 1:1 to IMRT (60-66 Gy) with cetuximab (C) (loading dose 400 mg/m^2 pre-RT plus weekly 250 mg/m^2 up to 11 total doses) (RT+C) or without C (RT). Patients were stratified by tumor site/ HPV status, clinical T-stage, EGFR expression level, and use of daily IGRT. The primary hypothesis was that RT+C would achieve superior overall survival (OS) in eligible patients. The trial was designed to detect a hazard ratio of 0.74 with 80% power, and 1-sided alpha of 0.025 (372 OS events, target enrollment of 700 patients). Disease-free-survival (DFS) and toxicity were secondary endpoints. Late toxicity was defined as >90 days after start of RT. OS and DFS between arms were compared via stratified log-rank test; toxicity was compared via Fisher's exact test. Locoregional failure was a tertiary/exploratory endpoint.

Results: The study enrolled 702 pts from 11/2009-3/2018; 627 were randomized, and 577 were eligible (287 RT and 290 RT+C). Most patients (64%) had oral cavity cancer, and 52% had clinical AJCCv6 stage IV(M0) cancer; a large majority (84.6%) had high EGFR expression. Due to substantially lower than expected event (death) rates, the protocol was amended to perform a time-driven analysis with data as of 06/05/2023 (184 OS events). At a median follow-up of 7.2 years, OS was not significantly improved, but DFS was (see table). Grade 3-4 acute toxicity rates were 70.3% (RT+C) versus 39.7% (RT), (p<0.0001), mostly related to skin and/or mucosal effects. Late Grade ≥3 toxicity rate was 33.2% (RT+C) versus 29.0% (RT) (p=0.3101). There were no Grade 5 toxicities in either arm.

Conclusion: Radiotherapy + cetuximab (RT+C) did not show OS superiority but significantly improved DFS, compared to RT alone for patients with resected, intermediate-risk SCCHN. Acute but not late toxicity was increased with RT+C. RT+C may be considered for this patient population, but it will be critical to identify subgroups achieving benefit from this combined-modality therapy.

LBA01 — Table 1

	5-year rates (%) [95% CI]			
	RT	**RT+C**	**HR [95% CI] [a]**	**p-value[c]**
OS	68.7 [63.1, 74.3]	76.5 [71.4, 81.6]	0.81 [0.60, 1.08]	0.0747
DFS	63.6 [57.8, 69.3]	71.7 [66.3, 77.1]	0.75 [0.57, 0.98]	0.0168
LRF	25.0 [20.0, 30.3]	19.3 [14.9, 24.3]	0.78 [0.56, 1.09] [0.63, 0.97] [b]	0.0746

[a]Stratified (cause-specific) Cox models; [b] 80% CI; [c] 1-sided

Acknowledgements: Support from NIH/NCI including grants U10CA180868 (NRG Oncology Operations), U10CA180822 (NRG Statistical Center), U24CA196067 (NRG Biospecimen bank); and from Eli Lilly Inc.

Author Disclosure: **M. Machtay**: Grant/research funding; NRG Oncology, RTOG Foundation. President of RTOG; RTOG. Deputy Chair; NRG. **P. Torres-Saavedra**: None. **W.L. Thorstad**: None. **P. Nguyen-Tan**: None. **L.L. Siu**: None. **F. Holsinger**: None. **A.K. El-Naggar**: None. **C.H. Chung**: None. **J. Dorth**: None. **N.Y. Lee**: None. **J. Chan**: None. **N. Dunlap**: None. **V. Bar Ad**: None. **W.A. Stokes**: None. **A. Chakravarti**: None. **D. Sher**: None. **S.S. Rao**: None. **J. Harris**: None. **S.S. Yom**: Grant/research funding; Bristol Myers Squibb, EMD Serono. Honoraria; Elsevier, ASTRO. book chapter royalty; Up To Date, Springer. **Q. Le**: Honoraria; Nanobiotix, Coherus. Travel expenses; Coherus, Roche/Genentech. Leading RTOGF group for clinical trials; NRG Oncology/ RTOGF.

LBA 02

Randomized Controlled Trial of Hypofractionated vs. Normo-fractionated Accelerated Radiation Therapy with or without Cisplatin for Locally Advanced Head and Neck Squamous Cell Carcinoma (HYPNO)

S.M. Bentzen,[1] E. Rosenblatt,[2] T. Gupta,[3] J.P. Agarwal,[3] S. Ghosh Laskar,[3] S. Bhasker,[4] A.A. Jacinto,[5] P. De Marchi,[5] M. Nagarajan,[6] K. Jabeen,[7] S. Binia,[8] Y. Chansilpa,[9] M. Napoles,[10] S. Aguiar,[11] O. Goloubeva,[12] E. Zubizarreta,[2] K. Hopkins,[2] and M. Abdel-Wahab[2]; [1]*Department of Radiation Oncology, University of Maryland School of Medicine, Baltimore, MD,* [2]*International Atomic Energy Agency, Vienna, Austria,* [3]*Department of Radiation Oncology, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India,* [4]*All India Institute of Medical Sciences, New Delhi, India,* [5]*Barretos Cancer Hospital, Sao Paolo, Brazil,* [6]*V.N. Cancer Centre, Coimbatore, India,* [7]*Bahawalpur Inst. of Nuclear Medicine and Oncology, Bahawalpur, Pakistan,* [8]*Fundación Escuela de Medicina Nuclear, Mendoza, Argentina,* [9]*Siriraj Hospital, Mahidol University, Bangkok, Thailand,* [10]*Instituto de Oncología y Radiobiología, Havana, Cuba,* [11]*Centro Hospitalario Pereira Rossell, Montevideo, Uruguay,* [12]*Epidemiology and Public Health, Univ. of Maryland, Baltimore, MD*

Purpose/Objective(s): HYPNO, a multi-center, two-arm, unblinded phase III trial, tested definitive hypofractionated (HFX) vs. normofractionated (NFX) accelerated RT ±cisplatin for locally advanced HNSCC. HYPNO opened in 12 centers in 10 low- and middle-income countries. We hypothesized HFX (55 Gy, 20F, 5F/wk over 4 weeks) is non-inferior to NFX (66 Gy, 33F, 6F/wk over 5.5 weeks) ± weekly cisplatin with a non-inferiority margin, Δ, chosen as an absolute difference of 10% at 3 years for the coprimary endpoints of loco-regional control (LRC) and Grade 3+ late adverse events (LAE). Chosen Δ corresponds to critical hazard ratios of 1.31 (LRC) and 1.5 (LAE).

Materials/Methods: 792 pts. were centrally randomized Mar 2014 to Feb 2020, 395 to HFX, 397 to NFX. Accrual closed, with all outcome data still blinded, with 792 of a planned 836 pts. (94.7%) enrolled, in part due to the emerging COVID-19 pandemic, in part due to accrual leveling off. Chemoradiation, prescribed before randomization, consisted of i.v. cisplatin 35 mg/m2 weekly during RT, 4 cycles in HFX arm, 5 in NFX arm. Stratification factors (distribution): Performance status 0-1 v. 2 (3.7%); Chemotherapy n v. y (75.8%); Tumor subsite: oral cavity (8.5%) v. oropharynx (50.5%) v. hypopharynx (13.5%) v. larynx (24.5%) v. other (3.0%), and institution. Enrollees were 86.9% males; 38.1% current and 39.3% former smokers; T3-4 (72.7%); N2-3 (49.1%). HYPNO allowed institutions to use their standard clinical RT technique: 2D (22.5%) v. 3D (7.1%) v. IMRT (70.2%). 3-year Kaplan-Meier estimates were used for time-to-event outcomes and compared with the log-rank test based on full follow-up time available.

Results: 3-year outcomes (see table). HFX was non-inferior for the coprimary endpoints. For LRC, HR=1.098, 95% CI (0.929, 1.298), non-inferiority p=0.041. For LAE G3+, HR=0.926, 95% CI (0.684, 1.253), non-inferiority p=0.004. Regarding early adverse events, max grade of mucositis was 3+ in 190/373 (50.9%) of cases after HFX and 208/380 (54.7%) after NFX, Fisher's Exact Test p=0.307.

Conclusion: HYPNO shows hypofractionated accelerated RT is non-inferior to the 6-fractions-a-week schedule with respect to both loco-regional tumor control and Grade 3+ late adverse events. In addition to passing the non-inferiority test, the 3-year outcomes were remarkably similar with an absolute difference of <1.5% between the two arms. This result is potentially practice changing. Treating in 20 fractions instead of 33 is both resource sparing and more convenient to patients. HYPNO is, to the best of our knowledge, the largest randomized controlled trial with this level of complexity conducted in the setting of low- and middle-income countries.

	OS	PFS	LRC	Late G3+ AEs
HFX	54.1±2.7%	44.0±2.6%	50.7±2.7%	18.8±2.4%
NFX	55.5±2.6%	45.3±2.6%	51.2±2.7%	20.2±2.4%
P-value	0.62	0.42	0.40	0.68

Author Disclosure: **S.M. Bentzen:** Guidelines of measurements of ionizing radiation; ICRU. **E. Rosenblatt:** None. **T. Gupta:** None. **J. Agarwal:** None. **S. Ghosh Laskar:** None. **S. Bhasker:** None. **A.A. Jacinto:** Medical Society; Brazilian Society of Radiation Therapy. **P. De Marchi:** None. **M. Nagarajan:** None. **K. Jabeen:** None. **S. Binia:** None. **Y. Chansilpa:** None. **M. Napoles:** None. **S. Aguiar:** None. **O. Goloubeva:** None. **E. Zubizarreta:** None. **K. Hopkins:** None. **M. Abdel-Wahab:** Global oncology; ASTRO.

LBA 03

5-Year Outcomes from PACE B: An International Phase III Randomized Controlled Trial Comparing Stereotactic Body Radiotherapy (SBRT) vs. Conventionally Fractionated or Moderately Hypo Fractionated External Beam Radiotherapy for Localized Prostate Cancer

N. van As,[1] A. Tree,[1] J. Patel,[2] P. Ostler,[3] H. Van Der Voet,[4] D.A. Loblaw,[5] W. Chu,[6] D. Ford,[7] S. Tolan,[8] S. Jain,[9] J.G. Armstrong,[10,11] P. Camilleri,[12] K. Kancherla,[13] J. Frew,[14] A. Chan,[15] O. Naismith,[1] G. Manning,[2] S. Brown,[2] C. Griffin,[2] and E. Hall[2]; [1]*The Royal Marsden NHS Foundation Trust, London, United Kingdom,* [2]*The Institute of Cancer Research, Clinical Trials and Statistics Unit, London, United Kingdom,* [3]*Mount Vernon Cancer Centre, Northwood, United Kingdom,* [4]*The James Cook University Hospital, Middlesbrough, United Kingdom,* [5]*Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada,* [6]*Sunnybrook Health Sciences Centre, Toronto, ON, Canada,* [7]*Queen Elizabeth Hospital, Birmingham, United Kingdom,* [8]*The Clatterbridge Cancer Centre, Liverpool, United Kingdom,* [9]*Queen's University Belfast, Belfast, United Kingdom,* [10]*Cancer Trials Ireland, Dublin, Ireland,* [11]*St Luke's Radiation Oncology Network, Dublin, Ireland,* [12]*Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom,* [13]*University Hospitals Leicester, Leicester, United Kingdom,* [14]*Freeman Hospital, Newcastle, United Kingdom,* [15]*University Hospitals Coventry and Warwickshire, Coventry, United Kingdom*

Purpose/Objective(s): External beam radiotherapy (EBRT) is a curative treatment for Localized Prostate Cancer (LPCa). Large randomized controlled trials (RCTs) have shown moderately hypo fractionated regimens (2.5 − 3 Gy/fraction(f)) as non-inferior to 2Gy/f regimens. PACE-B aims to demonstrate non-inferiority of SBRT compared to conventionally or moderately hypo fractionated regimens for biochemical and/or clinical failure (BCF).

Materials/Methods: PACE (NCT01584258) is an international phase III open-label multiple-cohort RCT. Men with LPCa, stage T1-T2, ≤ Gleason 3 + 4, PSA ≤ 20 ng/mL, unsuitable for surgery or preferring EBRT, were eligible. Participants (pts) were randomized (1:1) to SBRT (36.25 Gy / 5f in 1-2 weeks (wks)) or control radiotherapy (CRT) (78 Gy / 39 f over 7.5 wks, or 62 Gy / 20 f in 4 wks) to the planning target volume. Androgen deprivation therapy was not permitted. The primary endpoint was freedom from biochemical (BF)/clinical (CF) failure. BF is based on PSA rises, commencement of ADT or date of orchiectomy and CF is based on local recurrence, nodal recurrence, distant metastases and death from prostate cancer. 858 pts were needed to rule out 6% inferiority (80% power, one-sided alpha 5%) assuming 85% event-free rate with CRT, corresponding to a critical hazard ratio (HR) of 1.45. Analysis was done by intention to treat.

Results: 874 pts were randomized from 38 centers (n=441 (CRT) and n=433 (SBRT)) between 08/2012 and 01/2018. Baseline characteristics were well balanced across CRT and SBRT groups: median age 69.8 years (IQR 65.4,74.0); median PSA ng/mL (IQR): 8.1 (6.3,11) vs 7.9 (5.5,10.9); NCCN risk group 9.3% low, 90.7% intermediate. With median follow-up of 73.1 months (IQR 62.6, 84.0), 5-year BCF event free-rate (95% CI) was 94.6% (91.9% - 96.4%) vs 95.7% (93.2% - 97.3%) for CRT and SBRT groups respectively. SBRT was non inferior to CRT with unadjusted HR (90% CI) = 0.74 (0.47 - 1.17), p-value for non-inferiority=0.007. The estimated absolute differences in the proportion of patients event free in the SBRT group compared with that in the CRT group at 5 years was: 1.36% (90% CI: 0.87 - 2.80). At 5 years, RTOG grade 2 or worst (G2+) genitourinary toxicity was seen in 3.2% (11/348) pts who received CRT and 5.5% (20/363) pts who received SBRT (p=0.14); RTOG G2+gastrointestinal toxicity was seen in 1/348 receiving CRT and 1/363 received SBRT (p=0.99).

Conclusion: Five-year BCF free rates are high in PACE-B participants. After median follow-up of six years, five-fraction-SBRT is non-inferior to CRT for BCF. SBRT reduces pts attendances, shortens treatment time and 5 fraction SBRT should be a new standard of care for pts with low/favourable intermediate risk LPCa.

Author Disclosure: **N. van As**: Grant/research funding; Accuray, Varian. Honoraria; Accuray, Varian. Professor of Precision Prostate Radiotherapy; The Institute of Cancer Research. Medical Director; The Royal Marsden. **A. Tree**: Grant/research funding; Elekta, Accuray, Varian. Honoraria; Elekta, Janssen. Travel expenses; Elekta. Salary support; Elekta. Committee member; UK SABR consortium. Lead editor for GU at the red journal, which is financially compensated; IJROBP. I receive no direct compensation but my employer receives financial compensation to back fill my. **J. Patel**: Grant/research funding; Accuray. **P. Ostler**: None. **H. Van Der Voet**: None. **D. Loblaw**: President; Dr Loblaw Medicine Professional Corp. Advisory board; Astellas, Bayer. Copyright/Patent/License/Royalty; GU-Lok. GU Disease Site Chair; Sunnybrook Health Sciences Centre. Founder, Board Chair; Prostate Cure Foundation. **W. Chu**: Independent Contractor; Sunnybrook Health Sciences Center. Assistant professor; University of Toronto. **D. Ford**: None. **S. Tolan**: Travel expenses; Janssen. Conference fee paid; Janssen. **S. Jain**: Grant/research funding; Boston Scientific. Honoraria; Astra Zeneca, Janssen. Compensation/Payment; Boston Scientific. Board member; Friends of the Cancer centre. **J.G. Armstrong**: Independent Contractor; Beacon. Salary support; Health Beacon. Stock; Health Beacon, Elekta. **P. Camilleri**: Honoraria; ViewRay Inc. Uncompensated; University of Oxford. Limited liability company interest; Banna Medical Services. **K. Kancherla**: None. **J. Frew**: None. **A. Chan**: Honoraria; Advanced Accelerator Applications. **O. Naismith**: None. **G. Manning**: Grant/research funding; Accuray. **S. Brown**: Grant/research funding; Accuray. **C. Griffin**: Grant/research funding; Accuray. **E. Hall**: Grant/research funding; Accuray, Varian, Astrazeneca, Janssen-Cilag, Bayer, Roche Products Ltd, Merck Sharp and Dohme.

LBA 04

Primary Endpoint Results of NRG CC003: Phase IIR/III Trial of Prophylactic Cranial Irradiation (PCI) with or without Hippocampal Avoidance (HA) for Small Cell Lung Cancer (SCLC)

V. Gondi,[1] S. Pugh,[2] M.P. Mehta,[3] J.S. Wefel,[4] W.A. Tome,[5] A. Sun,[6] G.M. Videtic,[7] B.H. Lok,[8] H.A. Yoon,[9] J.H. Heinzerling, II[10] A.S. DeNittis,[11] R.C. McGarry,[12] K. Devisetty,[13] V. Kundapur,[14] A.J. Wu,[15] R. Paulus,[16] and L.A. Kachnic[17]; *[1]Northwestern Medicine Cancer Center Warrenville and Proton Center, Warrenville, IL, [2]NRG Oncology Statistics and Data Management Center, Philadelphia, PA, [3]Florida International University, Herbert Wertheim College of Medicine, Miami, FL, [4]The University of Texas MD Anderson Cancer Center, Houston, TX, [5]Institute for Onco-Physics, Albert Einstein College of Medicine, Bronx, NY, [6]Radiation Medicine Program, Princess Margaret Cancer Center, University of Toronto, Toronto, ON, Canada, [7]Department of Radiation Oncology, Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, [8]Department of Radiation Oncology, University of Toronto, Toronto, ON, Canada, [9]Cancer Care Specialists of Illinois, Decatur, IL, [10]Levine Cancer Institute, Atrium Health and Southeast Radiation Oncology Group, Charlotte, NC, [11]Lankenau Institute for Medical Research, Wynnewood, PA, [12]University of Kentucky, Lexington, KY, [13]Wayne State University/McLaren Cancer Institute, Flint, MI, [14]Saskatoon Cancer Centre, Saskatoon, SK, Canada, [15]Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center, New York, NY, [16]NRG Oncology Statistics and Data Management Center, Philadelphia, PA, [17]Columbia University, New York, NY*

Purpose/Objective(s): Prior randomized trials have demonstrated neurocognitive function (NCF) benefits of HA during whole-brain radiotherapy for non-SCLC brain metastases. NRG CC003 sought to evaluate whether HA confers similar neuroprotection and non-inferior intracranial relapse (ICR) risk following PCI for SCLC.

Materials/Methods: SCLC patients (pts) were stratified by age, stage and planned memantine use, and randomized to PCI or HA-PCI (25Gy in 10 fractions). Standardized NCF tests of Hopkins Verbal Learning Test-Revised (HVLT-R), Trail Making Tests (TMT), and Controlled Oral Word Association (COWA) were performed at baseline, 3, 6, 12, 18 and 24 months (mos). The primary endpoints were 12-mo ICR (phase II) and 6-mo HVLT-R Delayed Recall (DR) failure, defined as decline using the reliable change index (phase III). To detect a 14.5% reduction in 6-mo HVLT-DR failure, 196 analyzable pts were required for 80% power and one-sided α=0.05. Phase III sample size was increased to 392 pts for non-compliance and death. Secondary endpoints were first failure in any NCF test and failure in other NCF tests. NCF failure was analyzed using Fisher's exact test and mixed effects models. Cumulative incidence estimated time to NCF failure (death without NCF failure was competing risk); between-arm comparison tested using Cox proportional hazards model.

Results: From 12/2015-6/2022, 392 pts were randomized; study closed from 10/2017-7/2020 for phase IIR analysis. Median age was 64. 70% had limited stage; 47% used memantine. Median follow-up was 14.9 mos (all pts) and 24 mos (alive pts). Grade≥3 toxicity did not differ. HA-PCI had non-inferior 12-mo ICR rate (PCI 14.8% vs. HA-PCI 14.2%, p<0.0001 to rule out inferiority). 6-mo HVLT-R DR deterioration was not significant (PCI 30.0% vs. HA-PCI 26.0%, p=0.31). Addition of HA to PCI prevented NCF failure (adjusted HR=0.77, 95% confidence interval (CI): 0.61-0.98, p=0.03). Memantine use trended to increased NCF failure (adjusted HR=1.26, 95% CI: 0.99-1.59, p=0.062); test for interaction between HA and memantine use was non-significant. HA-PCI arm had higher COWA scores at baseline (mean: PCI 31.9 vs. HA-PCI 34.4, p=0.019) and exhibited greater deterioration in COWA over time (estimate -0.259, p=0.042). There were no differences in overall survival (adjusted HR=0.83, 95% CI: 0.63-1.09, p=0.19).

Conclusion: While the study did not meet its HVLT-DR failure primary endpoint, HA during PCI prevents NCF failure with non-inferior ICR risk and similar survival. The NCF benefit of HA was independent of non-significant higher NCF failure risk with memantine use. Worse verbal word fluency, assessed using COWA, following HA-PCI requires further investigation given baseline between-arm imbalance in COWA scores. Supported by grants UG1CA189867 (NCORP) and U24CA180803 (IROC) from the NCI.

Author Disclosure: **V. Gondi**: Partner; Radiation Oncology Consultants, LLC. Uncompensated; Novocure. Chair; NRG Oncology. **S. Pugh**: None. **M.P. Mehta**: Compensation/Payment; Kazia Therapeutics, Novocure. **J.S. Wefel**: Salary support; GT Medical Technology. Compensation/Payment; Bayer. Lead; International Cognition and Cancer Task Force. **W.A. Tome**: None. **A. Sun**: Honoraria; AstraZeneca. Co-Chair; Canadian Clinical Trials Group. **G.M. Videtic**: None. **B.H. Lok**: Grant/research funding; AstraZeneca, Pfizer. Honoraria; AstraZeneca. Travel expenses; AstraZeneca. **H.A. Yoon**: Partner; Cancer Care Specialists of Illinois. **J.H. Heinzerling**: Partner; SERO Group. Grant/research funding; AstraZeneca, VisionRT. **A.S. DeNittis**: Independent Contractor; Main Line Health. **R.C. McGarry**: Honoraria; Veteran's Administrationn. **K. Devisetty**: Independent Contractor; Radiation Research & Consulting, Coastal Retina Institute. Honoraria; Philips Healthcare, Establishment Labs. Compensation/Payment; Radialogica, Hologic, Establishment Labs. Stock; Abbott Laboratories, Abbvie. **V. Kundapur**: None. **A.J. Wu**: Grant/research funding; CivaTech Oncology, Inc. Honoraria; Nanovi A/S. Compensation/Payment; Simphotek, Inc. Stock options; Simphotek, Inc. **R. Paulus**: None. **L.A. Kachnic**: Grant/research funding; Varian Medical Systems. Honoraria; UpToDateTM. Compensation/Payment; New Beta Innovation. Uncompensated; RTOG. Liason to the group chair for the surgical, radiation, and imaging committees.; SWOG. Supervise design, conduct, analysis and budget of clinical community cancer prevention and control trials.; NRG Oncology.

LBA 05

Patient-Reported and Toxicity Results from the FABREC Study: A Multicenter Randomized Trial of Hypofractionated vs. Conventionally-Fractionated Postmastectomy Radiation Therapy after Implant-Based Reconstruction

J.S. Wong,[1] H. Uno,[2] A. Tramontano,[2] C. Pellegrini,[2] J.R. Bellon,[1] M.D. Cheney,[3] P.H. Hardenbergh,[4] A.Y. Ho,[5] K.C. Horst,[6] J.N. Kim,[7]

K.L. Leonard,[8] M.S. Moran,[9] C.C. Park,[10] A. Recht,[11] R. Shiloh,[12] A.G. Taghian,[13] L. Warren,[14] J.L. Wright,[15] Y. Chun,[16] and R.S. Punglia[17]; *[1]Dana-Farber/Brigham and Women's Cancer Center, Boston, MA, [2]Dana-Farber Cancer Institute, Boston, MA, [3]Harvard Radiation Oncology Program, Boston, MA, United States, [4]Shaw Regional Cancer Center; Medical Director of Radiation Oncology, Edwards, CO, [5]Department of Radiation Oncology, Duke University Medical Center, Durham, NC, [6]Department of Radiation Oncology, Stanford University School of Medicine, Stanford, CA, [7]Department of Radiation Oncology, University of Washington, Seattle, WA, [8]Department of Radiation Oncology, Rhode Island Hospital, Lifespan Cancer Institute, Warren Alpert Medical School of Brown University, Providence, RI, [9]Department of Therapeutic Radiology, Yale School of Medicine, New Haven, CT, [10]University of California San Francisco, Department of Radiation Oncology, San Francisco, CA, [11]Beth Israel Deaconess Medical Center, Boston, MA, [12]Department of Radiation Oncology, Dana-Farber Cancer Institute and Brigham & Women's Hospital, Boston, MA, [13]Harvard Medical School, Boston, MA, [14]Department of Radiation Oncology, Dana-Farber Cancer Institute, Boston, MA, [15]Johns Hopkins Medicine, Department of Radiation Oncology, Baltimore, MD, [16]Brigham and Women's Hospital, Boston, MA, [17]Department of Radiation Oncology, Dana-Farber Cancer Institute and Brigham and Women's Hospital, Boston, MA*

Purpose/Objective(s): This randomized trial of fractionation after breast reconstruction (FABREC) sought to compare quality-of-life (QOL) and clinical outcomes of hypofractionated (HF) vs. conventionally-fractionated (CF) postmastectomy radiation therapy (PMRT) in the setting of immediate prosthetic reconstruction.

Materials/Methods: Between 3/2018 and 11/2021, 400 patients at 18 centers with Stage 0-III breast cancer and immediate placement of tissue expander (TE) or implant (I) after mastectomy were randomized 1:1 to HF or CF photon PMRT. Respective doses in the two arms were 42.56 Gy/16 fractions to the chest wall (CW), with or without axillary/supraclavicular lymph node (LN) radiation (39.9 Gy/15 fractions) and 50 Gy in 25 fractions to CW (46-50 Gy to axillary LNs). A boost was not permitted; bolus was used at physician discretion. CW toxicity was defined as any grade ≥3 adverse event (CTCAE) after PMRT initiation. Patients were censored at study withdrawal or at diagnosis of distant recurrence. Participants completed QOL instruments (FACT-B, BREAST-Q, Lymph-ICF) at baseline, 6, 12 and 18-months from PMRT initiation. Questions regarding financial burden were included with the 6-month survey. Primary endpoint of the study was improvement in the Physical Well-Being (PWB) domain of FACT-B at 6 months with pre-specified stratification by age (younger than 45 vs. 45 years or older). QOL scores were compared using Student's t-test.

Results: Median follow-up for the 385 patients analyzed was 31.8 months (range, 6.9-54.4); median age was 47.0 years (range, 23-79). Preoperative chemotherapy was used in 67.8% and preoperative endocrine therapy (ET) in 21.5% of the cohort. There were 16 distant (8 in each arm), and 2 local-regional (1 in each arm) recurrences. CW toxicity occurred in 35 patients (19 HF, 16 CF, p=0.58) at medians of 3.4 and 4.8 months after RT initiation in the HF and CF arms, respectively (p=0.82). Post-operative infection before RT (HR=3.31, p=0.03), irradiation of TE vs I (HR=7.74, p=0.046), preoperative endocrine therapy (HR=3.45, p=0.0007) and number of LNs removed (HR=1.06/node, p=0.02) were significant for developing CW toxicity on multivariate analysis, while fractionation was not (HF HR=1.19, p=0.63). There was no significant difference in overall change in PWB scores at 6 months between the two treatment arms (p=0.71) or separately in younger (p=0.15) and older cohorts (p=0.27). However, HF patients younger than 45 were less bothered by side-effects of treatment (p=0.045) and nausea (p=0.02) vs. CF patients younger than 45. Among patients who took unpaid time off from work during treatment (n=51), those receiving HF required fewer hours off than those receiving CF (73.7 vs. 125.8, p=0.046).

Conclusion: Physical well-being and overall toxicity profile of HF PMRT were comparable between HF and CF PMRT. HF was associated with better 6-month QOL in some domains among younger patients. Our early results support the use of HF PMRT in the setting of TE- or implant-based breast reconstruction.

Author Disclosure: **J.S. Wong**: Honoraria; Wolters Kluwer. **H. Uno**: None. **A. Tramontano**: None. **C. Pellegrini**: None. **J.R. Bellon**: Honoraria; uptodate, varian, PER. Advisory task force to the NCI on local therapy protocols for breast cancer; NCI. Oral exam chair; American Board of Radiology. section editor; IJROBP. **M.D. Cheney**: Partner; Spectrum Healthcare Partners. N/A; Spectrum Healthcare Partners. **P.H. Hardenbergh**: Ownership equity; Chartrounds.org. **A.Y. Ho**: Grant/research funding; Merck, GSK. Honoraria; Merck. Consultant for Radiation Dermatitis; La Roche Posay. **K.C. Horst**: None. **J.N. Kim**: None. **K.L. Leonard**: Medical Staff; Lifespan/Rhode Island Hospital. Honoraria; Elsevier. N/A; The American College of Radiation Oncology Inc. **M.S. Moran**: Faculty; Yale School of Medicine. N/A; NCCN. Associate editor; Breast Cancer Research Tx. **C.C. Park**: None. **A. Recht**: Honoraria; EviCore, Exact Sciences. Uncompensated; Imagine Scientific, Inc. Stock; Imagine Scientific, Inc. **R. Shiloh**: None. **A.G. Taghian**: None. **L. Warren**: None. **J.L. Wright**: Employee; National Institutes of Health. Grant/research funding; Oncospace, Prostate Cancer Foundation. Honoraria; ASTRO, Physicians Education Resource, Elsevier Journals. Travel expenses; Physicians Education Resource. Salary support; Oncospace, Prostate Cancer Foundation. Compensation/Payment; Up To Date, Marshall Dennehy. Conduct oral e. **Y. Chun**: Grant/research funding; Surgical Innovation Associates. Compensation/Payment; Integra. **R.S. Punglia**: None.

LBA 06

Enzalutamide or Placebo Plus Leuprolide Acetate and Enzalutamide Monotherapy in Men with High-Risk Biochemically Recurrent Prostate Cancer and Prior Radiotherapy: EMBARK Subgroup Analysis

S. Sridharan,[1] N. Shore,[2,3] B. Venugopal,[4] M. Gleave,[5] U. De Giorgi,[6] Y. Tang,[7] G.P. Haas,[8] M. Rosales,[8] F. Zohren,[9] and S.J. Freedland[10,11]; *[1]Calvary Mater Newcastle Hospital, Waratah, NSW, Australia, [2]Carolina Urologic Research Center, Myrtle Beach, SC, [3]GenesisCare US, Myrtle Beach, SC, [4]University of Glasgow, Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom, [5]Vancouver Prostate Centre, University of British Columbia, Vancouver, BC, Canada, [6]IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) Dino Amadori, Medola, Italy, [7]Pfizer, Inc., San Francisco, CA, [8]Astellas Pharma, Inc., Northbrook, IL, [9]Pfizer, Inc., Cambridge, MA, [10]Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA, [11]Durham VA Medical Center, Durham, NC*

Purpose/Objective(s): The primary analysis of EMBARK demonstrated that after a median follow-up of 60.7 months metastasis-free survival (MFS) for enzalutamide (enza) + leuprolide acetate (LA; hazard ratio [HR] 0.42; 95% confidence interval [CI], 0.30−0.61; p<0.0001) and enza monotherapy (mono; HR 0.63; 95% CI, 0.46−0.87; p=0.0049) was clinically meaningful and statistically superior to placebo + LA. Here, we present a subgroup analysis of MFS by prior radiotherapy (RT).

Materials/Methods: EMBARK (NCT02319837) is a phase 3 study of patients with high-risk biochemical recurrence (BCR): prostate-specific antigen (PSA) doubling time ≤9 months and PSA ≥2 ng/mL above nadir post-RT or ≥1 ng/mL after radical prostatectomy (RP) ± postoperative RT. Patients were randomized (1:1:1) to enza 160 mg/day + LA (double-blind), placebo + LA (double-blind), or enza mono (open-label). LA 22.5 mg was administered every 12 weeks. If PSA was <0.2 ng/mL at Week 36, treatment was suspended at Week 37 and restarted when PSA was ≥2 ng/mL for patients with primary RP, and ≥5 ng/mL for patients without RP. The primary endpoint, determined by blinded, independent central review (BICR), was MFS with enza + LA vs placebo + LA. MFS of enza mono vs placebo + LA was a key secondary endpoint. Subgroup analysis of MFS by prior RT (yes/no) was pre-specified and considered descriptive.

Results: Overall, 804 patients received prior RT (enza + LA, n=265; placebo + LA, n=283; enza mono, n=256). External beam RT was the most common prior RT received (enza + LA, n=253 [71.3%]; placebo + LA, n=267 [74.6%]; enza mono, n=240 [67.6%]). For patients with prior RT, MFS per BICR for enza + LA and for enza mono were each superior to placebo + LA (**Table 1**). For patients without prior RT, MFS per BICR for enza + LA was superior to placebo + LA; there was no difference between the enza mono and placebo + LA cohorts (**Table 1**).

Conclusion: In patients with high-risk BCR and prior RT, both enza + LA and enza mono demonstrated a clinically meaningful improvement in MFS vs placebo + LA. In patients without prior RT, the number of MFS events was too low to draw any conclusions. If approved, enza combination therapy may represent a new standard of care for patients with high-risk BCR and prior RT.

LBA 06 − Table 1. MFS per BICR

	Enza + LA (n=355)	Placebo + LA (n=358)	Enza mono (n=355)
Prior RT (yes)			
n	265	283	256
Events	37	76	43
Median (95% CI). months	NR (NR−NR)	85.1 (80.1−NR)	NR (NR−NR)
HR (95% CI)	0.45 (0.30−0.66)	−	0.57 (0.39−0.82)
Nominal p-value	<0.0001	−	0.0025
Prior RT (no)			
n	90	75	99
Events	8	16	20
Median (95% CI), months	NR (NR−NR)	NR (NR−NR)	NR (NR−NR)
HR (95% CI)	0.37 (0.16−0.87)	−	0.93 (0.48−1.79)
Nominal p-value	0.0169	−	0.8259

NR, not reached

Clinical trial registration number: NCT02319837.

Author Disclosure: **S. Sridharan**: None. **N. Shore**: Partner; Atlanta Urology Clinics. Compensation/Payment; AbbVie, Accord, Alessa Therapeutics, Amgen, Antev, Arquer, Asieris, Astellas, AstraZeneca, AuroBiosciences, Bayer, BMS, Bioprotect, Boston Scientific, CGoncology, Clarity, Dendreon, Exact Imaging, Fize Medical, Genetech/Roche, Ferring, Foundation Medicine. Pharmacy/research; GenesisCa. **B. Venugopal**: Honorary Clinical Senior Lecturer; University of Glasgow. Honoraria; Ipsen, BMS, Merck Sharp and Dohme, EISAI. **M. Gleave**: Grant/research funding; Astellas, AstraZeneca, Janssen, Bayer, Sanofi, Pfizer, Tersera, Roche. Honoraria; Astellas, AstraZeneca, Janssen, Bayer, Sanofi, Pfizer, Tersera, Roche. Copyright/Patent/License/Royalty; Sustained Therapeutics. Founder; Sustained Therapeutics. **U. De Giorgi**: Honoraria; Pfizer, Astellas. **Y. Tang**: Stock; Pfizer Inc. **G.P. Haas**: None. **M. Rosales**: None. **F. Zohren**: None. **S.J. Freedland**: Honoraria; Pfizer, Astellas, Bayer, Merck, Sanofi, Myovant, Janssen.

LBA 07

Stereotactic Radiotherapy vs. Whole Brain Radiation Therapy for Patients with 1-10 Brain Metastases from Small Cell Lung Cancer: Results of the Randomized ENCEPHALON (ARO 2018-9) Trial

D. Bernhardt,[1] R. El Shafie,[2,3] M. Thomas,[4] F. Bozorgmehr,[5] A. Schiele,[2] D. Schmitt,[2,3] T. Welzel,[2] P. Thalmann,[6] A. Paul,[2] L. König,[2] K. Lang,[2] S. Adeberg,[2,7] S. Höne,[8] F. Weykamp,[2] P. Vollmuth,[9] A. Lentz-Hommertgen,[2] C. Jaekel,[10] U. Nestle,[11,12] M. Kieser,[6] J. Debus,[13,14] and S. Rieken[2,3]; *[1]Department of Radiation Oncology, Heidelberg University Hospital & Department of Radiation Oncology, Klinikum rechts der Isar, Technical University of Munich, Heidelberg, Germany, [2]Heidelberg University Hospital, Dept. of Radiation Oncology, Heidelberg, Germany, [3]University Medical Center Göttingen (UMG), Dept. of Radiation Oncology, Göttingen, Germany, [4]Department of Thoracic Oncology, Thoraxklinik and National Center for Tumor diseases (NCT) Heidelberg, Heidelberg University Hospital, Heidelberg, Germany, [5]German Center for Lung Research (DZL), Heidelberg, Germany, [6]Heidelberg University Hospital, Institute of Medical Biometry, Heidelberg, Germany, [7]University Medical Center of Gießen and Marburg (UKGM), Dept. of Radiation Oncology, Marburg, Germany, [8]Department of Radiation Oncology, Heidelberg University Hospital, Heidelberg, Germany, [9]University Hospital Heidelberg, Department of Neuroradiology, Heidelberg, Germany, [10]University Hospital Heidelberg, Department of Radiation Oncology, INF 400, Heidelberg, Germany, [11]Department of Radiation Oncology, Medical Center, Faculty of Medicine, University of Freiburg, Freiburg, Germany, [12]Kliniken Maria Hilf, Department of Radiation Oncology, Moenchengladbach, Germany, [13]Department of Radiation Oncology, University of Heidelberg, Heidelberg, Germany, [14]CCU Translational Radiation Oncology, German Cancer Research Center (DKFZ), National Center for Radiation Oncology (NCRO), Heidelberg Institute for Radiation Oncology (HIRO), Heidelberg, Germany*

Purpose/Objective(s): Although SRT is preferred for limited brain metastases from most histologies, WBRT has remained the standard of care for patients with SCLC. It remains unclear whether the benefit of WBRT to SRT for the intracerebral tumor control outweighs the potential neurocognitive risks in SCLC patients.

Materials/Methods: This pilot-trial is a single-center prospective, randomized, two-arm Phase II study. The primary endpoint is neurocognition after cerebral irradiation in SCLC patients treated with WBRT or SRT (radiosurgery (SRS) with 20 Gy or 18 Gy or hypofractionated SRT with 30 Gy in 5 Gy fractions for lesions >3 cm) defined as a drop of at least 5 points from baseline in Hopkins Verbal Learning Test−Revised (HVLT-R) total recall subscale at 3 months after baseline. Eligible patients had histologically confirmed SCLC, MRI-confirmed cerebral metastasis (not resected, maximum number of 10), Karnofsky performance score >50 and no prior irradiation to the brain. Patients were randomly assigned (1:1) to either SRT or WBRT. Secondary endpoints included survival parameters, quality of life, toxicity and neurocognitive assessments.

Results: 56 patients were randomized to either WBRT or SRT. The modified intention-to-treat (mITT) set included all randomized patients, who started study treatment with WBRT (n=25) or SRT (n=26). Prior to imputation, the primary endpoint was reached in 7.7% (n=2) of patients in the SRT group and 24.0% (n=6) of patients in the WBRT group (mITT set). After multiple imputation via predictive mean matching, the primary endpoint was analyzed using the Cochrane-Mantel-Haenszel test stratified for time of appearance (p=0.0723). For preliminary OS analysis in the mITT set, data up to 6 months were considered. Patients not having reached the endpoint were censored at 181 days. There was no significant difference in survival probability between treatment groups (p=0.36). Median time to death (at 6 months) was 124.0 (Q1 43.0- Q3 139.5) days in the SRT group and 131.0 (Q1 107.0-Q3 150.0) in the WBRT group.

Conclusion: SCLC patients in the WBRT group were at a greater risk of a significant decline in neurocognitive function 3 months after baseline compared with the SRT group. SRT should be considered one of the standards of care for patients with brain metastases from SCLC.

Author Disclosure: **D. Bernhardt**: Grant/research funding; Accuray. Honoraria; ASTRAZeneca, Novocure, Accuray. Travel expenses; Novocure, Accuray. Compensation/Payment; ASTRAZeneca, Novocure. Ownership equity; NEED Inc. **R. El Shafie**: Grant/research funding; Accuray, Novocure, AstraZeneca, BMS, Merck KG. Honoraria; Accuray, Novocure, AstraZeneca, BMS, Merck KG. Travel expenses; Accuray, Novocure, AstraZeneca, BMS, Merck KG. **M. Thomas**: None. **F. Bozorgmehr**: None. **A. Schiele**: None. **D. Schmitt**: None. **T. Welzel**: None. **P. Thalmann**: None. **A. Paul**: None. **L. König**: Honoraria; Novocure. Travel expenses; Novocure. **K. Lang**: None. **S. Adeberg**: Grant/research funding; MerckKGaA, Novocure, BMS, MSD, Accuray, AstraZeneca. Honoraria; MerckKGaA, Novocure, BMS, MSD, Accuray, AstraZeneca. Travel expenses; MerckKGaA, Novocure, BMS, MSD, Accuray, AstraZeneca. **S. Höne**: None. **F. Weykamp**: Honoraria; MSD, AstraZeneca. Travel expenses; AstraZeneca. **P. Vollmuth**: None. **A. Lentz-Hommertgen**: None. **C. Jaekel**: None. **U. Nestle**: Honoraria; ASTRAZeneca. Travel expenses; ASTRAZeneca. **M. Kieser**: None. **J. Debus**: Grant/research funding; Elekta, Raysearch. Honoraria; Elekta, Raysearch. Travel expenses; Elekta, Raysearch. **S. Rieken**: Grant/research funding; AstraZeneca GmbH, onkowissen.de GmbH. Honoraria; AstraZeneca GmbH, onkowissen.de GmbH. Travel expenses; AstraZeneca GmbH, onkowissen.de GmbH.

LBA 08

Acute Toxicity and Efficiency Outcomes in the DARTBOARD Randomized Trial of Daily Adaptive Radiotherapy for Head and Neck Squamous Cell Carcinoma

D.J. Sher,[1] V. Avkshtol,[2] M.H. Lin,[1] R. Hughes,[3] J. Wang,[4] M. Dohopolski,[3] J. Van Pelt,[3] C.Y. Liao,[3] and D.H. Moon[2]; [1]*Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX,* [2]*University of Texas Southwestern Department of Radiation Oncology, Dallas, TX,* [3]*University of Texas Southwestern Medical Center, Dallas, TX,* [4]*UT Southwestern Medical Center, Dallas, TX*

Purpose/Objective(s): The clinical utility of adaptive radiotherapy (ART) for head and neck (H&N) squamous cell carcinoma (SqCC) remains poorly defined. Online daily ART (DART) promises both anatomic adaptation and planning target volume (PTV) reduction by developing a unique plan based on the anatomy at each fraction, rendering interfraction setup error negligible. In this prospective trial using CBCT-based ART, patients with H&N SCC undergoing definitive RT (+/- chemotherapy, CRT) were randomized to daily online DART with reduced PTV margins (DART arm) or standard PTV margins without ART (IGRT arm).

Materials/Methods: Eligibility criteria included a diagnosis of oropharynx, larynx, or hypopharynx SqCC receiving definitive RT or CRT. All individuals received involved nodal radiotherapy (INRT) per a previous institutional study. The gross tumor volume (GTV) received 70 Gy, the primary clinical target volume (CTV) and suspicious nodes received 63 Gy, and nodes on the same level as nodal GTV or identified by an artificial intelligence (AI) algorithm received 56 Gy. The PTV margin in the DART arm was 1mm (2mm S/I), compared to 5mm in the IGRT arm. A H&N radiation oncologist adapted each DART fraction. The primary endpoint was patient-reported xerostomia at one year, requiring enrollment of 50 patients, stratified by oropharynx versus larynx/hypopharynx site. Patients completed the EORTC QLQ30/HN35, MDADI, and the Xerostomia Questionnaire (XQ) patient-reported outcome (PRO) instruments at baseline/1/3/6/12 months after treatment.

Results: Fifty patients were enrolled (26 IGRT, 24 DART). The cohort consisted of 38 oropharynx and 12 larynx/hypopharynx patients, with AJCC 7th stage I-II (n=4), III (n=10), and IVA/B (n=36). Forty-six patients (92%) were treated with CRT. The mean ipsilateral (16.0 vs. 11.5 Gy, p=0.02) parotid gland and ipsilateral (56.3 vs. 42.2 Gy, p<0.01) and contralateral (36.5 vs. 28.2 Gy, p=0.04) submandibular gland doses were significantly lower with DART. Swallowing OAR doses were not significantly different. The mean total patient in-room, recontouring, and physician at-console times were 33 (SD 5.3), 12.6 (SD 3.4), and 22 (SD 4.4) minutes per adaptive fraction, respectively. There was significantly less G2+ dermatitis in the DART arm (Grade 2+ 31% vs 8%, p=0.05) but not mucositis or dysphagia. No PRO differences were noted at one month, but at three months, trends favored reduced xerostomia with DART (XQ 43.1 vs. 31.2, p=0.2; for oropharynx patients, XQ 45 vs. 28.6, p=0.11). At a median follow-up of 7 months, one in-field, one out-of-field, and two distant recurrences were observed.

Conclusion: Online DART for H&N SqCC may improve physician- and patient-reported acute toxicity profiles, albeit with increased resource utilization. Additional evidence and follow-up is needed to understand the potential benefits and limitations of this paradigm.

Author Disclosure: **D.J. Sher**: Grant/research funding; Varian Medical Center. Copyright/Patent/License/Royalty; US. **V. Avkshtol**: None. **M. Lin**: None. **R. Hughes**: None. **J. Wang**: None. **M. Dohopolski**: Copyright/Patent/License/Royalty; US. **J. Van Pelt**: None. **C. Liao**: None. **D.H. Moon**: Grant/research funding; Gateway For Cancer Research, The Cary Council.

LBA 09

Stereotactic Ablative Body Radiotherapy (SABR) for Oligoprogressive ER-Positive Breast Cancer (AVATAR): A Phase II Prospective Multicenter Trial

S.P. David,[1] S. Siva,[2] M. Bressel,[3] J. Tan,[4] G.G. Hanna,[5] R.K. Alomran,[6] E. Yip,[7] C. Morton,[7] M. Edmonds,[7] and M. White[8]; [1]*Peter MacCallum Cancer Centre, Melbourne, VIC, Australia,* [2]*Peter MacCallum Cancer Centre and Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, Australia,* [3]*Peter MacCallum Cancer Centre and Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, VIC, Australia,* [4]*Peter MacCallum Cancer Centre, Melbourne, Australia,* [5]*Patrick G Johnston Centre for Cancer Research, Belfast, United Kingdom,* [6]*Department of Radiation Oncology, Comprehensive Cancer Center, King Fahad Medical City, Riyadh, Saudi Arabia,* [7]*Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia,* [8]*Monash Medical Centre, Melbourne, Australia*

Purpose/Objective(s): To assess if stereotactic ablative body radiotherapy (SABR) for oligoprogressive luminal (ER positive, Her-2 negative) advanced breast cancer could delay a change in combination CDK 4/6 inhibitor and an aromatase inhibitor therapy (CDK 4/6 + AI) by ≥ 6 months in > 25% of patients. Herein we report the primary outcome.

Materials/Methods: AVATAR (ACTRN 12620001212943) enrolled eligible patients with advanced luminal breast cancer who received first or second line systemic treatment in the metastatic setting with a CDK 4/6 + AI for ≥ 6 months. Patients required an ECOG performance status of 0-2 and 1-5 extracranial oligoprogressing lesions amenable to SABR. Patients who had chemotherapy for metastatic disease, leptomeningeal disease, or prior radiotherapy to an oligoprogressing lesion planned for SABR were excluded. At subsequent progression, further SABR was permitted to delay a change in systemic therapy. The primary endpoint was event free survival (EFS) defined as a time to change in systemic therapy after SABR, any progression within 6 months or in > 3 lesions. Secondary endpoints were progression free survival (PFS), overall survival (OS), treatment related toxicity and modified progression free survival (mPFS) defined as progression not amenable to further SABR at any time.

Results: 32 patients were recruited (Aug 2020 − Nov 2022), with a median follow-up of 15.8 months. The number of patients with 1, 2, 3, or 4 sites of oligoprogression at baseline was 13 (41%), 10(31%), 7 (22), and 2 (6%), respectively. The most common sites of oligoprogression were bone 44 (71%), and nodal 11 (18%). The most common SABR doses were 20 Gy /1 fraction and 24 Gy/2 fractions. The null hypothesis was rejected, with 47% (95% CI: 29-65) of patients remaining event free for ≥ 6 months. The median mPFS was 10.4 months (95% CI: 4.1-not reached) with 46% (95% CI: 27-63) remaining unchanged on systemic therapy for 12 months. Median PFS was 5.2 months (95% CI: 3.1-6.8), with 10/30 (33%) progressions suitable for a second course of SABR for oligoprogression to further delay systemic therapy change. 17 (53%) patients had no treatment related toxicity. 13 (40%) and 2 (13%) patients experienced grade 1 or 2 treatment related toxicities respectively, with no grade 3 or higher toxicities reported.

Conclusion: This is the first prospective trial investigating SABR as a strategy to maintain CDK 4/6 + AI in patients with oligoprogessive luminal breast cancer. This approach was well tolerated, with a higher than anticipated median time to change in systemic therapy of 10.4 months, and 46% of patients maintained on a CDK 4/6 + AI for 12 months. These findings suggest that patients with oligoprogressive luminal breast cancer should be considered for SABR in lieu of a change in systemic therapy.

Author Disclosure: **S.P. David**: Grant/research funding; Roche Genentech. **S. Siva**: payment to institution; Reflexion Medical Systems. Payment to institution; AstraZeneca, Varian Medical Systems. volunteer role for advisory of the board; Radiosurgery Society (RSS). advisory role; ART committee of IASLC. **M. Bressel**: Honoraria; Sir Peter MacCallum Department of Oncology, University of Melbourne. Provide advice; Australia New Zeland Gynaecological Oncology group. **J. Tan**: None. **G.G. Hanna**: Travel expenses; MSD. Compensation/Payment; AstraZeneca. **R.K. Alomran**: Honoraria; MESTRO. **E. Yip**: None. **C. Morton**: Management advisory consultant; Open Advisory. **M. Edmonds**: None. **M. White**: Honoraria; Pfizer, Gilead. Provide advice; Breast Cancer Network Australia.

LBA 10

Partial Breast Radiotherapy for Women with Early Breast Cancer: 10-Year Outcomes from IMPORT LOW (CRUK/06/003)

A. Kirby,[1,2] C. Griffin,[3] L. Finneran,[3] M. Sydenham,[3] A. Alhasso,[4] A.M. Brunt,[5] H. Chan,[6] M. Jefford,[7] E. Sawyer,[8] I. Syndikus,[9] Y.M. Tsang,[10] D. Wheatley,[11] J. Yarnold,[12] C. Coles,[13] and J. Bliss[3]; [1]*The Royal Marsden Hospital NHS Foundation Trust, London, United Kingdom,* [2]*Institute of Cancer Research, London, United Kingdom,* [3]*The Institute of Cancer Research, Clinical Trials and Statistics Unit, London, United Kingdom,* [4]*Beatson West of Scotland Cancer Centre, Glasgow, United Kingdom,* [5]*University Hospital of North Midlands, Stoke-on-Trent, United Kingdom,* [6]*Nuffield Health Cheltenham Hospital, Cheltenham, United Kingdom,* [7]*Independent Cancer Patient's Voice, London, United Kingdom,* [8]*Guys & St Thomas' Foundation Trust, King's College, London, United Kingdom,* [9]*The Clatterbridge Cancer Centre, Department of Radiotherapy, Wirral, United Kingdom,* [10]*Mount Vernon Cancer Centre, Northwood, United Kingdom,* [11]*Royal Cornwall Hospital, Truro, United Kingdom,* [12]*Division of Radiotherapy and Imaging, the Institute of Cancer Research, London, United Kingdom,* [13]*University of Cambridge, Cambridge, Cambridges, United Kingdom*

Purpose/Objective(s): IMPORT LOW is a randomized, multi-center phase III trial testing partial breast radiotherapy (RT) using intensity modulated RT in women with early-stage breast cancer at lower than average risk of ipsilateral breast tumor relapse (IBTR). Five-year results concluded non-inferiority for reduced-dose & partial-breast RT with similar normal tissue effects (reduced for breast appearance & hardness as reported by patients; Lancet, 2017). Here we report outcomes after 10 years.

Materials/Methods: Women age ≥50 who had breast conservation surgery, for invasive breast cancer (excluding classical lobular carcinoma) pT1-2 (≤3cm) N0-1, any grade, with microscopic margins of ≥2 mm, were eligible. Patients were randomized (1:1:1) to 40Gy/15F to whole breast (control); 36Gy/15F to whole breast & 40Gy/15Fr to partial breast (reduced-dose); or 40Gy/15F to partial breast (partial-breast). The primary endpoint is IBTR. 10-year clinician assessed adverse effects were collected. Patient assessments were not recorded at 10 years. Efficacy analysis was intention to treat.

Results: 2016 patients were recruited from 05/2007 to 09/2010 from 30 UK RT centers (674 control, 673 reduced-dose, 669 partial-breast). Median age was 63 years (IQR 57-68); 42%, 48% & 10% of patients had tumors that were grade 1, 2 & 3 respectively; 3% were node positive. Median follow-up is 121 (IQR 120-124) months. 10-year follow-up forms were received for 518, 520 & 510 whole, reduced & partial groups respectively. 10-year rates of IBTR are 2.8% (95%CI 1.8-4.5), 1.9% (1.1-3.4) & 2.8% (1.7-4.5) in the whole-breast, reduced-dose & partial-breast groups respectively. Absolute treatment differences in IBTR compared with control for reduced-dose is -1.02% (95%CI -1.97, 0.96) & -0.02% (-1.38, 2.58) for partial-breast. 10-year overall survival rates are 87.8% (95%CI 84.9, 90.1), 87.2% (84.3, 89.6) & 90.3% (87.7, 92.4) for control, reduced-dose & partial-breast groups respectively. Clinician assessed adverse effects indicate low rates of moderate/marked events at 10 years (Table 1).

Conclusion: At 10 years, rates of IBTR & clinician assessed moderate/marked adverse effects remain very low across all treatment groups demonstrating that reduced-dose & partial-breast RT are safe & effective RT techniques.

LBA 10 – Table 1: Proportion of patients with none/mild & moderate/marked clinician assessed adverse effects at 10 years

Year 10		Whole-breast n (%)	Reduced-dose n (%)	Partial-breast n (%)
Breast shrinkage	None/mild Moderate/marked	290 (91) 29 (9)	293 (91) 28 (9)	307 (94) 21 (6)
	P-value*		0.89	0.30
Breast induration (index)	None/mild Moderate/marked	304 (96) 12 (4)	304 (95) 16 (5)	313 (96) 12 (4)
	P-value*		0.56	0.45
Telangiectasia	None/mild Moderate/marked	305 (99) 2 (1)	316 (100) 0	320 (100) 0
	P-value*		0.24	0.99
Breast oedema	None/mild Moderate/marked	306 (99) 1 (1)	313 (99) 2 (1)	319 (99) 1 (1)
	P-value*		0.99	0.62

(*Continued*)

* P-value compared with whole-breast

Author Disclosure: **A. Kirby**: Travel expenses; ESTRO Society. Travel costs for ESTRO-related matters covered by ESTRO; European Society of Radiotherapy and Oncology. **C. Griffin**: Grant/research funding; Accuray Inc. Compensation/Payment; Institute of Cancer Research MSc in Oncology. **L. Finneran**: None. **M. Sydenham**: None. **A. Alhasso**: None. **A. Brunt**: None. **H. Chan**: Board member; Federation of Independent Practitioners. **M. Jefford**: None. **E. Sawyer**: Grant/research funding; Pfizer, Seagen. **I. Syndikus**: Honoraria; Bayer, Jansen. Travel expenses; Bayer, Jansen. **Y. Tsang**: Faculty; University of Toronto. Committee Chair; ESTRO. **D. Wheatley**: None. **J. Yarnold**: retired; retired. **C. Coles**: Grant/research funding; National Institute of Health & Care Research (NIHR). Director; CRUK RadNet Cambridge. Chair of breast cancer commission; Lancet Breast Cancer Commission. **J. Bliss**: Grant/research funding; Astra Zeneca, GBG Forschungs GmbH, CRUK, JP Moulton Foundation, NIHR, Eli Lilly and Company Ltd, AstraZeneca UK Ltd, Merk, Sharp and Dohme Ltd, Verastem, Pfizer, PUMA, Kortuc, Lanssen Cilag Ltd. Member of the BIG Executive Board; Breast International group (BIG).

LBA 11

Early Results of a Phase I Pre-Operative Single Fraction Ablative Trial for Early Stage Breast Cancer

A.S. Rahimi,[1] M. Leitch,[2] B. Dogan,[3] P.G. Alluri,[1] D. Farr,[2] M. Arbab,[1] S. Seiler,[3] D.W.N. Kim,[4] R. Wooldridge,[2] N. Unni,[5] C.R. Nwachukwu,[1] I. Patel,[5] Y. Zhang,[1] D.D.M. Parsons,[1] A. Nguyen,[2] H.E. Morgan,[6] H.L. McArthur,[5] S. Sahoo,[7] and R.D. Timmerman[1]; [1]*University of Texas Southwestern Department of Radiation Oncology, Dallas, TX,* [2]*Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX,* [3]*Department of Radiology, University of Texas Southwestern Medical Center, Dallas, TX,* [4]*The University of Texas Southwestern Medical Center, Dallas, TX, United States,* [5]*University of Texas Southwestern Medical Center, Medical Oncology, Dallas, TX,* [6]*CARTI Cancer Center in Little Rock, Little Rock, AR,* [7]*Department of Pathology, University of Texas Southwestern, Dallas, TX*

Purpose/Objective(s): To explore the impact of pre-operative single fraction stereotactic ablative partial breast irradiation (SPBI) dose escalation (30, 34, or 38Gy) on toxicity and tumor response for early-stage hormone receptor (HR)+ breast cancer in an interim analysis of an expanded cohort phase I dose escalation study (NCT04040569).

Materials/Methods: Eligible patients (pts) have < 3 cm, HR+, Her2 -, cN0 invasive breast carcinomas not requiring chemotherapy. Pts are treated on either MR LINAC, robotic radiosurgery, or cobalt stereotactic breast units. Endocrine therapy is started two weeks after SPBI. Surgery is completed 2-12 months after SPBI. The primary objective is to escalate single fraction SPBI to an ablative dose without exceeding maximum tolerable dose (MTD). Secondary endpoints include pathologic complete response (pCR), local control, toxicity, cosmesis, and distant disease-free survival. Near complete response (nCR) is defined as RCB 1 and Miller-Payne 4/5. Dose limiting toxicity (DLT) is defined as grade ≥3 toxicity or any grade 4/5 toxicity attributed to SPBI. Each dose cohort enrolls 7-15 pts. Dose escalation is permitted if 0/7, 2/ 9, ≤3/12, or ≤4/15 patients experienced a DLT within 90 days of SPBI. MTD is exceeded if more DLTs occur in any cohort.

Results: From 12/2019 to 6/2023, 11 and 15 pts were treated with 30Gy and 34Gy, respectively. Rates of pCR/nCR are 37.5% for 30Gy versus 92.8% 34 Gy (p=0.01). At 30Gy, 8/11 pts (73%) underwent surgery with a median 4.3 (range 2.8-5.9) month interval from SPBI to surgery: 0/8 (0%) had a pCR and 3/8 (37.5%) had a nCR. At dose level 34Gy, 14/15 pts (93%) underwent surgery with a median 7.3 (range 5.9-12) month interval from SPBI to surgery: 6/14 (42.8%) had a pCR while 7/14 (50%) had a nCR. Of the 8 pts with a nCR, 50% had only 1-3mm of residual disease. The mean ki67 for the entire cohort was 12.0% +/- 6.9% at diagnosis and decreased to 1.4 +/-2.3% at surgery. 13/14 (92.8%) pts with residual disease had a ki67 < 3% after surgery and SPBI. There were 33 acute grade 1; 2 acute grade 2 (breast pain and dermatitis); and 10 late grade 1 [1 grade 2 (breast pain), and 1 grade 3 (slow healing wound) in an uncontrolled diabetic] toxicities.
Conclusion: First study to show pre-operative SPBI up to 34Gy in a single fraction was safe and effective for early-stage HR+ breast cancer. Escalating the dose has achieved a dramatic improvement in pCR/nCR (92.8%) suggesting this is an exciting approach for potentially eliminating tumor with radiation/endocrine therapy alone in early stage breast cancer and potentially paving a path towards non-surgical management in selected patients.

Author Disclosure: **A.S. Rahimi**: Grant/research funding; Accuray. Honoraria; Accuray, GE Health, Hologic. Travel expenses; Accuray. Compensation/Payment; Hologic. Guidelines; NCCN. **M. Leitch**: None. **B. Dogan**: Grant/research funding; Seno Medical, MedCognetics, NIH 5R37CA234428-02. Compensation/Payment; NIH UG1, NY state department of Health Peter T Rowley Breast Cancer Research Grant, Elsevier. **P. G. Alluri**: Grant/research funding; Department of Defense, METAvivor. Member; UT Southwestern Breast Center. **D. Farr**: None. **M. Arbab**: None. **S. Seiler**: None. **D. Kim**: None. **R. Wooldridge**: None. **N. Unni**: None. **C. R. Nwachukwu**: None. **I. Patel**: None. **Y. Zhang**: None. **D.D. Parsons**: None. **A. Nguyen**: None. **H.E. Morgan**: None. **H.L. McArthur**: Honoraria; Pfizer, Merck, AstraZeneca, Daiichi-Sankyo, Gilead. Travel expenses; Pfizer, Merck. **S. Sahoo**: None. **R.D. Timmerman**: Grant/research funding; Varian, Elekta, Accuray.

LBA 12

Stereotactic Radiosurgery for 1-10 Brain Metastases Avoids Whole-Brain Radiotherapy - Results of the CYBER-SPACE Randomized Phase 2 Trial

R. El Shafie,[1,2] D. Bernhardt,[3,4] A. Schiele,[1] T. Welzel,[1] D. Schmitt,[1,2] P. Thalmann,[5] S. Erdem,[1] A. Paul,[1] S.J. Hoene,[1] K. Lang,[1] L. König,[1] F. Weykamp,[1] S. Adeberg,[1,6] A. Lentz-Hommertgen,[1] C. Jaekel,[1] F. Bozorgmehr,[7,8] M. Thomas,[7,8] M. Kieser,[5] J. Debus,[1] and S. Rieken[1,2]; *[1]Heidelberg University Hospital, Dept. of Radiation Oncology, Heidelberg, Germany, [2]University Medical Center Göttingen (UMG), Dept. of Radiation Oncology, Göttingen, Germany, [3]Department of Radiation Oncology, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany, [4]Department of Radiation Oncology, Heidelberg University Hospital & Department of Radiation Oncology, Klinikum rechts der Isar, Technical University of Munich, Heidelberg, Germany, [5]Heidelberg University Hospital, Institute of Medical Biometry, Heidelberg, Germany, [6]University Medical Center of Gießen and Marburg (UKGM), Dept. of Radiation Oncology, Marburg, Germany, [7]Department of Thoracic Oncology, Thoraxklinik and National Center for Tumor diseases (NCT) Heidelberg, Heidelberg University Hospital, Heidelberg, Germany, [8]German Center for Lung Research (DZL), Heidelberg, Germany*

Purpose/Objective(s): Stereotactic Radiosurgery (SRS) is increasingly used as an alternative to whole-brain radiotherapy (WBRT) in the treatment of patients with multiple brain metastases (BM) with the aim of reducing toxicity and improving tumor control. The CYBER-SPACE trial evaluated SRS based on highly sensitive magnetic resonance imaging (MRI) for patients with 1-10 BM with the aim of avoiding or delaying WBRT.
Materials/Methods: Eligible patients with 1-10 newly diagnosed BM regardless of histology were randomized 1:1 to receive SRS of all visible lesions based on either SPACE (sampling perfection with application optimized contrasts using different flip angle evolution) or MPRAGE (magnetization-prepared rapid gradient-echo) MRI sequence. If during follow-up new BM occurred, SRS was repeated for those BM. The primary endpoint was ineligibility for further SRS. It was defined as the simultaneous new occurrence or progression of more than 10 BM or leptomeningeal disease. Key secondary endpoints were overall survival (OS), safety, quality of life and neurocognitive function.
Results: 202 patients were randomized; SPACE n = 99, MPRAGE n = 103. Most common histologies were non-small cell lung cancer (63%), melanoma (16%) and breast cancer (10%). At data cutoff after 24 months, the probability of ineligibility for further SRS (iffS), considering death as a competing event was 21.7% (95%-CI: 16.1%; 27.9%) in the overall cohort, 23.9% (95%-CI: 15.9%; 32.9%) in the MPRAGE arm and 19.4% (95%-CI: 11.8%; 28.3%) in the SPACE arm. Median time to iffS was not reached in either arm. There was no significant difference between SPACE and MPRAGE in time to iffS (p=0.411). In multivariable Cox-Regression, 5-10 BM (vs. 2-4 BM) on initial MRI were predictive for shorter time to iffS (HR 3.13, 95%-CI: 1.53; 6.40, p = 0.002). Median OS was 13.1 months (Q1-Q3: 5.2-44) in both groups combined, 10.5 months (Q1-Q3: 5.1-30.4) in the SPACE arm and 15.2 months (Q1-Q3: 5.6-45.0) in the MPRAGE arm, with no significant difference between arms (p=0.585). In multivariable Cox-Regression, predictors for longer OS were a Karnofsky Performance Status >80% (HR 0.51, 95%-CI: 0.33; 0.77, p = 0.002), concomitant immunotherapy (HR 0.34, 95%-CI: 0.23; 0.52, p < 0.001) or targeted therapy (HR 0.51, 95%-CI: 0.34; 0.78, p = 0.002), however not the initial number of BM. Cause of death was known for 108 of 138 patients (78.3%). 14 patients (10.1%) died from BM, 94 patients (68.1%) from extracranial causes.
Conclusion: SRS for patients with 1-10 BM avoided the need for WBRT in 79.2% of cases, when repeated upon occurrence of new lesions. Regular high-sensitivity MRI is a prerequisite for this strategy. Proactive management of multiple BM with SRS can greatly limit the impact of BM on overall prognosis.

Author Disclosure: **R. El Shafie**: Grant/research funding; Accuray Inc, Novocure, AstraZeneca, Bristol Myers Sqibb, Merck KGaA. Honoraria; Accuray Inc, Novocure, AstraZeneca, Bristol Myers Sqibb, Merck KGaA. Travel expenses; Accuray Inc, Novocure, AstraZeneca, Bristol Myers Sqibb, Merck KGaA. Stock; Novocure. **D. Bernhardt**: Grant/research funding; Accuray Inc. Honoraria; AstraZeneca, Novocure, Accuray Inc. Travel expenses; AstraZeneca, Novocure, Accuray Inc. **A. Schiele**: None. **T. Welzel**: None. **D. Schmitt**: Board member; German Society of Medical Physics (DGMP), German Society of Radiation Oncology (DEGRO). **P. Thalmann**: None. **S. Erdem**: None. **A. Paul**: None. **S.J. Hoene**: None. **K. Lang**: None. **L. König**: Honoraria; Novocure. Travel expenses; Novocure. **F. Weykamp**: Honoraria; AstraZeneca, MSD. Travel expenses; AstraZeneca, MSD. **S. Adeberg**: Grant/research funding; Merck KGaA, Novocure GmbH, Bristol Myers Squibb, MSD, Accuray Inc., AstraZeneca. Honoraria; Merck KGaA, Novocure GmbH, Bristol Myers Squibb, MSD, Accuray Inc., AstraZeneca. Travel expenses; Merck KGaA, Novocure GmbH, Bristol Myers Squibb, MSD, Accuray Inc., AstraZeneca. **A. Lentz-Hommertgen**: None. **C. Jaekel**: None. **F. Bozorgmehr**: None. **M. Thomas**: None. **M. Kieser**: None. **J. Debus**: None. **S. Rieken**: Grant/research funding; AstraZeneca. Honoraria; AstraZeneca. Travel expenses; AstraZeneca.

LBA 13

Hypofractionated Stereotactic Radiotherapy (HFSRT) of the Resection Cavity vs. Whole-Brain Radiotherapy (WBRT) Following Brain Metastasis Resection – Results of the ESTRON Randomized Phase 2 Trial

R. El Shafie,[1,2] D. Bernhardt,[3,4] A. Schiele,[2] T. Welzel,[2] D. Schmitt,[1,2] P. Thalmann,[5] S. Erdem,[2] A. Paul,[2] S.J. Hoene,[2] K. Lang,[2] L. König,[2] F. Weykamp,[2] S. Adeberg,[2,6] A. Lentz-Hommertgen,[2] C. Jaekel,[2] F. Bozorgmehr,[7,8] M. Thomas,[7,8] M. Kieser,[5] J. Debus,[2] and S. Rieken[1,2]; *[1]University Medical Center Göttingen (UMG), Dept. of Radiation Oncology, Göttingen, Germany, [2]Heidelberg University Hospital, Dept. of Radiation Oncology, Heidelberg, Germany, [3]Department of Radiation Oncology,*

Klinikum rechts der Isar, Technical University of Munich, Munich, Germany, [4]Department of Radiation Oncology, Heidelberg University Hospital & Department of Radiation Oncology, Klinikum rechts der Isar, Technical University of Munich, Heidelberg, Germany, [5]Heidelberg University Hospital, Institute of Medical Biometry, Heidelberg, Germany, [6]University Medical Center of Gießen and Marburg (UKGM), Dept. of Radiation Oncology, Marburg, Germany, [7]Department of Thoracic Oncology, Thoraxklinik and National Center for Tumor diseases (NCT) Heidelberg, Heidelberg University Hospital, Heidelberg, Germany, [8]German Center for Lung Research (DZL), Heidelberg, Germany

Purpose/Objective(s): Radiotherapy of the resection cavity following brain metastasis (BM) resection improves local control. Single-session stereotactic radiosurgery (SRS) can reduce toxicity compared to whole-brain radiotherapy (WBRT). Hypofractionated stereotactic radiotherapy (HFSRT) can deliver a higher biologically effective dose, potentially improving local control over SRS. The ESTRON trial compared HFSRT of the cavity with post-operative WBRT in patients with 1-10 BM.

Materials/Methods: Eligible patients with 1-10 newly diagnosed BM and following the resection of one BM regardless of histology were randomized 1:1 to receive HFSRT of the cavity and SRS of all unresected lesions or WBRT. A dose of 7 × 5 Gy was delivered to the cavity with a safety margin of 3-4 mm based on highly sensitive and standardized magnetic resonance imaging (MRI). The primary endpoint was intracranial control. Key secondary endpoints were overall survival (OS), safety, quality of life and neurocognitive function.

Results: 54 patients were randomized; HFSRT n=27, WBRT n=27. Most common histologies were non-small cell lung cancer (54%) and breast cancer (13%). Median cavity diameter was 28 mm (Q1-Q3: 22-33). 27 patients (52%) had at least one and 14 patients (26%) had >3 unresected BM. 15 patients (29%) had residual tumor at the cavity. These characteristics did not differ significantly between arms. At 12 months, intracranial control (IC) was 44% in the HFSRT and 59% in the WBRT arm. Median intracranial progression-free survival was 4.7 months (Q1-Q3: 1.7-18.0) in the HFSRT arm and 15.2 months (Q1-Q3: 5.6-12.7) in the WBRT arm (HR 1.72, 95%-CI: 0.94; 3.17, p = 0.080). In multivariable Cox-Regression, incomplete resection was predictive of inferior IC (HR 2.18, 95%-CI: 0.99; 4.79, p = 0.052). 3-year Local control (LC) at the cavity was 96% in the HFSRT arm and 89% in the WBRT arm (p=0.116) with a median follow-up of 19.7 months. Progression occurred distant from the cavity in 96% of cases (n = 26 out of 27). Leptomeningeal disease (LD) occurred in 7 patients (26%) in the HFSRT arm and 2 patients (7%) in the WBRT arm. LD occurred out of field in 6/7 cases in the HFSRT arm. 4 patients (15%) in the HFSRT arm and none in the WBRT arm developed blood brain barrier disruption at the cavity; 2 of those were symptomatic requiring treatment. Median OS was 10.3 months (Q1-Q3: 3.7-19.5) in the HFSRT arm and 18.6 months (Q1-Q3: 7.2-26.6) in the WBRT arm (HR 1.38, 95%-CI: 0.72; 2.66, p = 0.336).

Conclusion: Following the resection of BM, HFSRT of the resection cavity provides excellent local control. Compared to WBRT, distant intracranial progression and LD remain a relevant risk and rigorous follow-up is warranted. Detailed analyses on neurocognitive function are pending.

Author Disclosure: **R. El Shafie**: Grant/research funding; Accuray Inc, Novocure, AstraZeneca, Bristol Myers Sqibb, Merck KGaA. Honoraria; Accuray Inc, Novocure, AstraZeneca, Bristol Myers Sqibb, Merck KGaA. Travel expenses; Accuray Inc, Novocure, AstraZeneca, Bristol Myers Sqibb, Merck KGaA. Stock; Novocure. **D. Bernhardt**: Grant/research funding; Accuray Inc. Honoraria; AstraZeneca, Novocure, Accuray Inc. Travel expenses; AstraZeneca, Novocure, Accuray Inc. **A. Schiele**: None. **T. Welzel**: None. **D. Schmitt**: Board member; German Society of Medical Physics (DGMP), German Society of Radiation Oncology (DEGRO). **P. Thalmann**: None. **S. Erdem**: None. **A. Paul**: None. **S.J. Hoene**: None. **K. Lang**: None. **L. König**: Honoraria; Novocure. Travel expenses; Novocure. **F. Weykamp**: Honoraria; AstraZeneca, MSD. Travel expenses; AstraZeneca, MSD. **S. Adeberg**: Grant/research funding; Merck KGaA, Novocure, Bristol Myers Squibb, MSD, Accuray Inc., AstraZeneca. Honoraria; Merck KGaA, Novocure, Bristol Myers Squibb, MSD, Accuray Inc., AstraZeneca. Travel expenses; Merck KGaA, Novocure, Bristol Myers Squibb, MSD, Accuray Inc., AstraZeneca. **A. Lentz-Hommertgen**: None. **C. Jaekel**: None. **F. Bozorgmehr**: None. **M. Thomas**: None. **M. Kieser**: None. **J. Debus**: None. **S. Rieken**: None.

LBA 14

Diagnostic CT-Enabled Radiation Therapy (DART): Results of a Randomized Trial for Palliative Radiation Therapy

M. O'Neil,[1] J.M. Laba,[2] T. Nguyen,[1] M.I. Lock,[1] C.D. Goodman,[2] E. Huynh,[3] J. Snir,[4] V. Munro,[5] J.A. Alce,[5] L. Schrijver,[5] S. Lemay,[5] T. Macdonald,[5] A. Warner,[1] and D.A. Palma[1]; *[1]Department of Radiation Oncology, London Health Sciences Centre, London, ON, Canada, [2]London Health Sciences Centre, London, ON, Canada, [3]Department of Radiation Oncology, London Regional Cancer Program, London, ON, Canada, [4]London Regional Cancer Program, London Health Sciences Centre, London, ON, Canada, [5]London Regional Cancer Program, London, ON, Canada*

Purpose/Objective(s): The use of diagnostic CT (dCT) scans in place of CT simulation (CTsim) scans can increase departmental efficiency and reduce patient burden. The goal of the DART trial was to assess the impact of dCT-based planning on patient experience, plan deliverability, adequacy of target coverage, and staff workflows.

Materials/Methods: In this medical radiation therapist (MRT)-led trial, we enrolled patients undergoing same-day CTsim and treatment for palliative radiotherapy (PRT) to thoracic, abdominal, pelvic, or proximal limb targets. A recent dCT (within 28 days) in a reproducible position was required. After stratifying by target type (bone/soft tissue vs. visceral), patients were randomized in a 1:2 ratio between standard CTsim-based planning (control arm) vs. dCT-based planning (dCT arm). The primary endpoint was time in center (TIC), defined as the total time spent in the cancer center on the day of treatment, from first appointment to treatment delivery completion. Secondary endpoints included plan deliverability, adequacy of target coverage (scored by blinded physicians), and stakeholder acceptability (based on surveys of patients, MRTs, medical physicists and ROs).

Results: Accrual began in June 2022 and target accrual was reached in April 2023: 33 patients were enrolled with a total of 42 treatment sites. Median age was 72 (interquartile range [IQR]: 67-78), 73% were male, and the most common primary cancers were lung (33%), prostate (24%), and breast (12%). Treatment target volumes were bone/soft tissue metastasis for group 1 (n=25, 76%), and visceral (primary or metastatic) lesions for group 2 (n=8, 24%). The most commonly prescribed doses were 8 Gy in 1 fraction and 20 Gy in 5 fractions (50% and 43% of plans, respectively), and 91% of plans used parallel-opposed paired beams. Median time from dCT to enrollment date was 13 days (IQR: 8-22). The primary endpoint, TIC, was 4.8 ± 1.1 hours (mean ± SD) in the control arm vs. 0.4 ± 0.1 hours in the dCT arm (p<0.001). All plans were deliverable in the dCT arm. There were no differences in dose distribution acceptability rates, with all plans in both arms rated as "acceptable" (80% in control; 81% in dCT) or "acceptable with minor deviation" (20% in control; 19% in dCT). Patient perception of acceptability was similar in both arms with the exception of time burden, rated as "acceptable" by 50% in the control arm vs. 90% in the dCT arm (p=0.025). On a 5-point scale ranging from unacceptable (1) to acceptable (5), with 3 being neutral, the dCT workflow was rated as a 4 or higher by 90% of clinical stakeholders, including all ROs and medical physicists.

Conclusion: dCT-based radiation planning substantially reduced TIC without detriment in plan deliverability or quality and also reduced patient-reported time burden. dCT-based planning is a viable workflow and should be considered for patients with a recent diagnostic CT scan who are undergoing PRT.

Author Disclosure: **M. O'Neil**: None. **J.M. Laba**: Independent Contractor; London Health Sciences Centre. **T. Nguyen**: Independent Contractor; London Health Sciences Centre. Travel expenses; Non-profit. Stock options; NEED. **M.I. Lock**: Independent Contractor; London Health Sciences Centre. Honoraria; Knight Therapeutics, Abbvie, Tersera, Eisai. Stock; Myovant. **C. D. Goodman**: Independent Contractor; London Health Sciences Centre. Honoraria; Astra Zeneca. **E. Huynh**: None. **J. Snir**: None. **V. Munro**: None. **J.A. Alce**: None. **L. Schrijver**: None. **S. Lemay**: None. **T. Macdonald**: None. **A. Warner**: None. **D.A. Palma**: Independent Contractor; London Health Sciences Centre. Honoraria; UptoDate.com, Need Inc. Stock; Need Inc.