MODERN RADIOTHERAPY FOR HEMATOLOGIC MALIGNANCIES

February 16-17, 2019 • University of California, San Diego

Table of Contents

Planning Committee		See below
Index of Authors		See below
Abstracts		
1 – 5	Oral Abstracts	Pages 1-3
6	Publish Only	Page 3

All abstracts to be presented at the 2019 Modern Radiotherapy for Hematologic Malignancies are embargoed until the start of the meeting. The embargo policy applies to all abstracts regardless of whether information is obtained from another source.

Planning Committee

Bradford Hoppe, MD, MPH
Co-chair
University of Florida

Rahul R. Parikh, MD
Co-chair
Rutgers Cancers Institute of New Jersey

Andrea Ng, MD, MPH
Brigham and Women's Hospital

Bouthaina Dabaja, MD
MD Anderson Cancer Center

Joachim Yahalom, MD, FASTRO
Memorial Sloan Kettering Cancer Center

Parag Sanghvi, MD, MS
University of California, San Diego

Index of Authors

Bates, James	1
Goldberg, Eliana	3
Penagaricano, Jose	5
Pinnix, Chelsea	2
Tiwari, Anu	6
Wright, Ato	4

Co-sponsors:

ASTRO TARGETING CANCER CARE

ILROG INTERNATIONAL LYMPHOMA RADIATION ONCOLOGY GROUP

International Journal of Radiation Oncology biology • physics

www.redjournal.org

Hematologic Malignancies Abstracts

ORAL ABSTRACTS

1

Long-Term Outcomes in 10-Year Survivors of Early-Stage Hodgkin Lymphoma

J.E. Bates,[1] N.P. Mendenhall,[1] R.T. Hoppe,[2] L.S. Constine,[3] and B.S. Hoppe[4,5]; *[1]Department of Radiation Oncology, University of Florida College of Medicine, Gainesville, FL, [2]Stanford University School of Medicine, Stanford, CA, [3]Department of Radiation Oncology, University of Rochester Medical Center, Rochester, NY, [4]Department of Radiation Oncology, University of Florida College of Medicine, Jacksonville, FL, [5]University of Florida, Gainesville, FL*

Purpose/Objective(s): The progression-free survival benefit of radiotherapy (RT) in patients with early-stage Hodgkin lymphoma (HL) has been affirmed by numerous prospective trials. However, concerns regarding late RT effects have resulted in a decline in the use of RT in recent years. We aimed to investigate differences in overall survival (OS) among 10-year survivors of early-stage HL to further elucidate long-term treatment risks.

Materials/Methods: Using the Surveillance, Epidemiology, and End Results (SEER-18) database, we identified 9,017 10-year survivors of stage I-II HL initially treated between 1983 and 2004 of any age with histologic confirmation of disease and classical HL as their first malignant neoplasm. Kaplan-Meier and Cox proportional hazards analyses were used to determine relationships between treatment modality and cause of death. Diagnosis in 1995 or later was used as a surrogate for "modern treatment era" approximating the adoption of involved-field RT and ABVD chemotherapy.

Results: Of the 9,017 10-year survivors, 31.7% received chemotherapy alone, 27.6% received RT alone, and 40.8% received combined-modality therapy (CMT). Median age at diagnosis was 30 years (interquartile range [IQR], 22 − 40 years). Median follow-up from diagnosis was 15.6 years (IQR, 12.6 − 21.3 years). On multivariate analysis − including race, gender, age (using the median age, 30 years, as a binary cutoff), and modern RT era − 10-year survivors treated with CMT experienced improved OS relative to those treated with RT alone (HR = 1.44; 95% CI = 1.22 − 1.70; $p < 0.01$) and those treated with chemotherapy alone (HR = 1.31; 95% CI 1.10 − 1.56; $p < 0.01$). This was driven by an increase in death owing to non-HL causes; no differences were seen in HL-specific survival. Survivors treated in the modern era experienced improved OS relative to those diagnosed before 1995 but only if they were treated with CMT (HR = 0.70; 95% CI = 0.51 − 0.95; p = 0.02). There was no difference in survival by treatment era in those treated with RT alone (HR = 1.02; 95% CI = 0.78 − 1.34; p = 0.89) or chemotherapy alone (HR = 0.85; 95% CI = 0.65 − 1.13; p = 0.27).

Conclusion: Among 10-year survivors of early-stage HL, those treated with CMT experience improved OS and a decreased burden of death due to non-HL causes relative to survivors treated with chemotherapy or RT alone. Significant changes in RT field design and chemotherapy regimens for early-stage HL occurred in the mid-1990s; survivors treated with combined-modality treatment saw improvements in OS not seen by those treated with chemotherapy or RT alone. These results suggest that modern CMT, which has offered smaller RT fields and less-intense chemotherapy in tandem, offers diminished long-term toxicity relative to higher doses of either therapy.

Author Disclosure: **J.E. Bates**: None. **N.P. Mendenhall**: None. **R.T. Hoppe**: Employee; Stanford University. Honoraria; NCCN. ISCL. **L.S. Constine**: American College of Radiology. **B.S. Hoppe**: Research Grant; NRG. Travel Expenses; Children Oncology Group. Board Member; Proton Collaborative Group. Develop appropriateness criteria; American College of Radiology.

2

The Management of Primary Mediastinal B Cell Lymphoma Refractory to Dose-Adjusted R-EPOCH alone

C.C. Pinnix,[1] S.A. Milgrom,[1,2] J.R. Gunther,[1] L. Nastoupil,[3] and B. Dabaja[1]; *[1]The University of Texas MD Anderson Cancer Center, Division of Radiation Oncology, Houston, TX, [2]MD Anderson Cancer Center, Houston, TX, [3]University of Texas MD Anderson Cancer Center, Houston, TX*

Purpose/Objective(s): Primary mediastinal B-cell lymphoma (PMBCL) is a subtype of diffuse large B-cell lymphoma that generally affects young adults. Patients often present with bulky, symptomatic mediastinal masses. Until recently the standard of care therapy was doxorubicin based immune-chemotherapy followed by consolidative radiation therapy. In the United States many practitioners now elect for dose adjusted R-EPOCH immune-chemotherapy without planned RT based on encouraging phase 2 trial data with event free survival rates over 90%. The management of patients with refractory disease however can be challenging. We sought to examine the efficacy of various salvage treatment options as well as the outcomes of patients with relapsed and refractory disease after initial therapy with DA-R-EPOCH.

Materials/Methods: We performed a retrospective analysis of patients with newly diagnosed stage I-IV PMBCL treated between 2009 and 2015 at a single tertiary cancer center who had PET-CT scans before and after frontline therapy with DA-R-EPOCH who developed relapsed or refractory disease. We examined salvage therapy approaches and outcomes.

Results: We identified 10 patients that met eligibility criteria with a median follow up time of 3.4 years (range 1.3-7.3 years). The median age was 35 years (range 21-50), 60% were male. Ninety percent of patients had bulky disease at diagnosis. The site of relapsed or refractory disease was the mediastinum in all patients. Biopsy was performed to confirm refractory lymphoma in 6 cases. Eighty percent of patients received salvage chemotherapy (platinum based). Salvage radiation therapy was given to 80% of patients to a median dose of 43.6 Gy with intensity modulated radiation therapy (IMRT, n=7) or proton therapy (n=1). Eight patients underwent stem cell transplantation (autologous, n=4; allogeneic, n=4). 1 patient has died of disease.

Conclusion: Aggressive multi-modality salvage therapy can be successful in the management of PMBCL.

Author Disclosure: **C.C. Pinnix**: Research Grant; Merck & Co. Consultant; Global Oncology One. **S.A. Milgrom**: None. **J.R. Gunther**: None. **L. Nastoupil**: None. **B. Dabaja**: None.

3

Radiotherapy is an Effective Definitive Treatment for Limited Stage Grade 3A Follicular Lymphoma

E. Goldberg, B.S. Imber, K. Chau, E. Joffe, and J. Yahalom; *Memorial Sloan Kettering Cancer Center, New York, NY*

Purpose/Objective(s): While radiotherapy (RT) is established as a highly effective strategy for limited stage, grade 1-2 follicular lymphoma (FL), the treatment of grade 3A disease remains controversial. We sought to review outcomes of grade 3A patients treated definitively with RT.

Materials/Methods: We retrospectively reviewed 36 grade 3A FL patients (median age 62 years, 47% male) who received RT monotherapy between 2003-2018. Best post-RT imaging response was evaluated using Lugano criteria for all by CT, and by PET if available. Progression free survival (PFS) and overall survival (OS) were calculated using Kaplan Meier from first day of RT. Cox regression was used to analyze possible predictors of PFS.

Results: Patients received RT either definitively (n=25, 69%), as consolidation post excisional biopsy (n=9, 25%) or post surveillance (n=2, 6%). Patients were stage I (89%) or II (11%), 12 (33%) had extranodal disease and 2 (6%) had B symptoms. Common nodal sites included inguinofemoral (25%) and head and neck (25%). Planned RT dose was most commonly 36 Gy (39%) and ranged from 24-40 Gy. One patient terminated RT early for mucositis.

Post-RT CT response was available for 33 patients (92%) and most (n=29, 88%) had complete response (CR), 2 (6%) had partial response (PR) and 2 (6%) had an early out-of-field relapse (both biopsies confirmed as nodal low-grade FL). Post-RT PET response was available for 19 (53%); 16 (84%) had CR, 2 had PR and 1 had out-of-field relapse.

With median follow-up of 46 months we note 8 relapses (22%) with 1-, 2- and 5-year PFS of 94%, 84% and 73%, respectively. No significant predictors of PFS were found including demographics, stage, extranodal status, Ki67 score or RT dose. OS was excellent, with 2 deaths (6%), one of cardiac cause and one of unknown cause. Median time to relapse was 15.8 months (range 2.1-78.9). Relapses were out-of-field and biopsied as grade 3A FL (n=3), low-grade FL (n=3) and DLBCL (n=1); one patient had widespread in-field and out-of-field recurrence and was not re-biopsied. For salvage therapy, 3 received systemic therapy with no further relapse at the time of analysis, 2 were observed with no further relapse, 1 had excision and RT for two distant relapses without subsequent progression, 1 had RT to an additional site with further progression, and 1 was observed with further progression followed by systemic therapy with no additional relapse. No late toxicities attributable to RT were noted.

Conclusion: RT is a safe and highly effective treatment for low volume grade 3A FL, with similar outcomes to published series of low-grade histology. Relapses are predominantly distant from the RT field and most who relapse can be successfully salvaged with excellent survival. Given the possibility of late relapse, longer follow-up and prospective cohorts are warranted.

Author Disclosure: **E. Goldberg**: None. **B.S. Imber**: None. **K. Chau**: None. **E. Joffe**: None. **J. Yahalom**: None.

4

Successful treatment of debilitating back pain, in patient with polycythemia vera, with fractionated low-dose external-beam-radiation-therapy

A.O. Wright,[1] W.J. Kil,[1] and M. Khan[2]; *[1]Wellspan Health, Chambersburg, PA, [2]Summit Health Cancer Center, Chambersburg, PA*

Purpose/Objective(s): Bone pain as the presenting symptom in polycythemia vera (PV) is rare, especially without the diagnosis of myelofibrosis (MF). Pain, however, can manifest as a late symptom in approximately 50% of patients with the diagnosis. The cause of pain has been attributed to hematopoiesis, periostitis, and osteosclerosis. Pain is usually progressive and eventually refractory to pain regimens, and durable treatments are limited. Radiation therapy has been used in the management of different conditions associated with PV, including splenomegaly, extramedullary hematopoiesis, etc.

Materials/Methods: We present a case of an 82-year-old male who presented with lower back pain. MRI of the spine showed a mass in the anterior portion of the L2 vertebral body. A PET/CT scan showed a mildly hypermetabolic lesion along the anterior left half of the L2 vertebral body. He had a vertebroplasty and biopsy of the L2 vertebral body lesion and the pathology was diagnostic for mildly hypercellular marrow with trilineage hematopoiesis, and mildly increased polyclonal plasma cells. Bone marrow aspirate showed a mildly hypercellular marrow with maturing trilineage hematopoiesis with JAK2 mutation and no evidence of myelofibrosis and no flow cytometry abnormalities. Patient's low back pain was managed with narcotic pain medications for approximately 6 months, however the pain progressed and eventually was refractory to the narcotic pain medications. Patient presented for radiation oncology evaluation with complaints of 10/10, intense pain in the lumbar region, especially with ambulation. He was taking, oxycodone 5 mg every 4 hours. Patient received palliative radiation therapy, 5 Gy in 5 fractions, to a radiation field encompassing L1-L3.

Results: Patient responded very well to radiation therapy. Pain decreased to 2/10 in intensity after 2 Gy in 2 fractions, and he was able to discontinue pain medications after the 2nd fraction. By the completion of the 5 Gy dose, his pain had completely resolved. No treatment related toxicity was reported. At 2 months follow-up, patient reported durable pain relief and patient did not have to take any pain medications.

Conclusion: Pain associated with PV can be debilitating. Prior reports often adopted a single dose radiotherapy regimen, in the 5 -6 Gy range. With this L2 lesion, located between the kidneys and adjacent to the bowel, fractionation, we anticipated would help minimize the risk of normal tissue toxicity and provide flexibility for retreatment, given the refractory nature of associated pain. A limitation of this study is that we have one patient however, it is important to note that not only is this disease rare, but also, presentation with bone pain, without MF is also rare. Given the rarity of this disease, large scale prospective studies to validate the best approach for pain management would pose a major challenge.

Author Disclosure: **A.O. Wright**: None. **W. Kil**: None. **M. Khan**: None.

5

Robust Planning Reduces Toxicity in the Treatment of Head and Neck (HN) Pediatric Hodgkin's Lymphoma (PHL)

J.A. Penagaricano, X. Zhang, and G. Narayanasamy; *University of Arkansas for Medical Sciences, Little Rock, AR*

Purpose/Objective(s): PHL radiotherapy can cause delayed toxicity due to a large irradiated volume. Decreasing toxicity by reducing the volume of irradiated normal tissue is of interest (i.e., PTV elimination).

Robust optimization accounts for treatment set-up uncertainties during the dose optimization process. In robustness, the dose for multiple set-up error scenarios are computed and the treatment plans are optimized with respect to all scenario doses simultaneously. That is, the worst-case scenario satisfies the optimization problem.

The purpose of this work is to show proof-of-concept of robust optimization of HN-PHL.

Materials/Methods: Four CTVs (bilateral CTV1, unilateral CTV2, unilateral lower CTV3 and unilateral upper CTV4) were defined for a selected HN-PHL patient CT data set. CTV1, CTV2 and CTV4 were in close proximity to the parotid gland(s). CTV1 and CTV2 are involved field targets, and CTV3 and CTV4 are involved site targets. Three photon IMRT plans (PTV margin-based (referred as "plan1"), CTV robust-based ("plan2") and CTV plus parotid robust-based ("plan3")) were generated for each target. PTV was created by uniformly expanding the CTV by 0.5cm. Robust optimization plans were generated based on CTV set-up uncertainty of 0.5cm in all directions using identical optimization parameters as the margin-based plan. To evaluate for robustness, perturbed doses, with no CT density perturbation, were calculated with an iso-center shift of 0.25cm in all directions. Plans are considered robust if at least 95% of the prescribed dose covered at least 95% of the CTV. Dose was prescribed to 95% of the CTV or PTV to receive 21Gy in 14 fractions. Target (D_{95}) and OAR doses including normal tissue ring1 (4mm wide at 1cm from target) and ring2 (1cm extension from ring1) were compared. Student's t-test was performed to evaluate significance of differences in mean at a threshold p-value of 0.05.

Results: The target D_{95} satisfied the prescription for all plans. Perturbed dose calculation revealed that robustness was satisfied for plan2 and plan3. Plan1 produced significantly higher OAR doses as compared to plan2 and plan3 (p-value < 0.001). Comparing plan2 and plan3, the target dose coverage is comparable, and plan3 delivers lower dose to the parotid but the difference was not significant.

Conclusion: Robust and margin-based plans satisfy the prescribed target dose coverage. Robust plans show doses to be robust as intended. Robust optimization has added the advantage of sparing OARs as compared to margin-based plans especially when the target is adjacent to an OAR. Introducing robust objectives to OARs in addition to the target can further improve the sparing of normal tissue and potentially reduce toxicity.

Author Disclosure: **J.A. Penagaricano**: None. **X. Zhang**: None. **G. Narayanasamy**: None.

PUBLISH ONLY

6

Prevalence of depression and anxiety among cancer patients in small town in India: Single Centre study

A. Tiwari; *Royal Cancer Institute and Research Center, Kanpur, India*

Purpose/Objective(s): Depression and anxiety in cancer patients is a common comorbidity, therefore can deteriorate ones' Quality of Life. HADS (Hospital Anxiety and Depression Scale) is a reliable instrument used to asses these psychological issues. To assess the predominance of depression and anxiety, this review was conducted.

Materials/Methods: 401 Patients were screened, in our institute coming for follow up since 2011. Patients with history of advance malignancy were included. Among the patients 37% were female ,63% were males and different site are as 57% head & neck, 22% thorax, 13% GIT and 8% miscellaneous. In this study interviewee should be above 18yrs, have stamina for interview, Hindi or English speaking and most importantly, should be free form malignancy. A qualified interviewer administered the interview with the help of HADS. The questionnaire had 4 pointer scale for 14 items, which were further divided in Depression and Anxiety scale. Score between 0-7 were clinical normal, 8-10 were mild and 11-21 were clinical anxious and depressed.

Results: Among 401patients, 43% needed psychological and/or psycho-pharmacological intervention as they were highly depressed, the patients which were normal was 57%. While on Anxiety Scale 60% were either highly /mildly anxious, thus only 40% were normal. 52% of the female had depression and 69% had anxiety. On the other hand, 38% of male had depression and 45% had anxiety.

Conclusion: The research showed that most of the patients needed psychological and/or psycho-pharmacological intervention. Despite the completion of the treatment most of the patients experienced maladjustment or sub-clinical psychological issues

Author Disclosure: **A. Tiwari**: None.