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## **Extremely hypofractionated radiation therapy shows promising toxicity results for intermediate risk prostate cancer patients**

*Large Scandinavian trial finds comparable side effects at two years following 42.7 Gy delivered in seven fractions compared to 78 Gy delivered in 39 treatments*

BOSTON, September 26, 2016 -- For men with intermediate risk prostate cancer, side effects at two years following radiation therapy (RT) were comparable for extremely-hypofractionated treatment, which was delivered in seven fractions across two and a half weeks, and conventional treatment of 39 fractions across eight weeks, according to research presented today at the 58<sup>th</sup> Annual Meeting of the American Society for Radiation Oncology (ASTRO).

The HYPO-RT-PC trial, a randomized multi-institutional phase III trial in Scandinavia, was designed to assess outcomes from highly accelerated extreme hypofractionation, which is delivered in smaller number of high doses -- seven fractions of 6.1 Gy each in this study.

“Randomized trials have confirmed the value of radiation dose escalation for prostate tumors, and the potential benefits of larger radiation doses in fewer fractions, are expected to increase the therapeutic efficacy for men with prostate cancer,” said Anders Widmark, MD, a professor of radiation sciences at Umeå University in Umeå, Sweden and lead author of the study. “Most of the existing data on hypofractionation, however, draws on cases of moderately accelerated radiation treatment of the prostate, in contrast to our study with more extreme hypofractionation. Our trial shows that patients experience similar side effects at two years with *highly* accelerated extremely hypofractionation.”

Twelve hundred men with intermediate risk prostate cancer were enrolled in the HYPO-RT-PC non-inferiority trial between 2005 and 2015. Eligible patients presented with tumor stages of T1c to T3a,

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prostate-specific androgen (PSA) levels of 20 or below, and one or two of three risk factors: stage T3a, a Gleason tumor score of seven or higher, or a PSA level greater than 10.

Patients were randomized to one of two treatment arms: the conventional fractionation group (CF) received 78 Gy of image-guided RT to the prostate in 39 treatments of 2 Gy each over eight weeks, and the extreme hypofractionation group (E-HF) received 42.7 Gy in seven treatments of 6.1 Gy each over two and a half weeks. Most patients (80 percent) received three-dimensional conformal RT (3DCRT), and the remaining patients received volumetric arc therapy (VMAT). Androgen deprivation therapy was not allowed among study participants.

Primary outcomes included physician-reported side effects measured via a modified RTOG scale and patient-reported outcomes of urinary, bowel and sexual function side effects measured with the Prostate Cancer Symptom Scale (PCSS) questionnaire. Side effects were measured prior to RT start (baseline), at the end of RT, and at three, six, 12, 18 and 24 months following completion of RT. Median follow-up time from randomization for the entire patient population was 4.2 years, and findings reflect the 866 patients who reached two-year follow-up at the time of reporting in May 2016.

Men who received extremely hypofractionated RT in seven treatments experienced similar side effects two years following treatment as those who received conventional RT in 39 treatments. Rates of physician-reported grade 2+ toxicities at two years following treatment did not differ significantly between treatment arms. Urinary side effects were reported for 5.4 percent of E-HF patients and 4.6 of CF patients ( $p = 0.59$ ). Bowel side effects were reported for 2.2 percent of E-HF patients and 3.7 of CF patients ( $p = 0.20$ ). Impotence at two years post-treatment was reported in 34 percent of both groups, compared to 16 percent among all participants at baseline. Patient-reported outcomes at two years following treatment also did not differ significantly between treatment groups for overall bother from urinary ( $p = 0.17$ ), bowel ( $p = 0.12$ ) or sexual function ( $p = 0.71$ ) symptoms.

Some modest but statistically significant differences emerged between the accelerated and conventional treatment arms in shorter-term bowel and urinary side effects. Acute urinary toxicity immediately following treatment was similar for both treatment groups (27.6 percent for E-HF vs. 22.8 percent for C-HF,  $p = 0.11$ ), although acute bowel toxicity at the end of RT was higher for the accelerated E-HF treatment than for CF (9.4 vs. 5.3 percent;  $p = 0.023$ ). Patient-reported bowel function at the end of RT was also significantly worse following E-HF than following CF for seven of 10 symptoms assessed, although these differences dissipated at three and six months follow-up. At one year post-treatment, patient-reported urinary function was significantly worse among E-HF patients for four of the 14 symptoms measured.

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“The trial was designed to have equal late toxicity, so although there were some differences in shorter-term side effects, the results for long-term toxicity were precisely what we hoped to find,” said Dr. Widmark. “Our plan moving forward is to analyze primary endpoint data and present updated toxicity results approximately one year from now.”

The abstract, “Extreme Hypofractionation vs. Conventionally Fractionated Radiotherapy for Intermediate Risk Prostate Cancer: Early Toxicity Results from the Scandinavian Randomized Phase III Trial “HYPO-RT-PC”,” will be presented in detail during a scientific session at ASTRO’s 58th Annual Meeting at 7:45 a.m. Eastern time on Tuesday, September 27, 2016. To speak with Dr. Widmark, please contact ASTRO’s media relations team on-site at the Boston Convention and Exhibition Center September 25 through 28, by phone at 703-286-1600 or by email at [press@astro.org](mailto:press@astro.org).

**ATTRIBUTION TO THE AMERICAN SOCIETY OF RADIATION ONCOLOGY (ASTRO) ANNUAL MEETING REQUESTED IN ALL COVERAGE.**

Full study abstract available on the final page of this release.

**ABOUT ASTRO’S ANNUAL MEETING**

*ASTRO’s 58th Annual Meeting, the nation’s premier scientific meeting in radiation oncology, will be held September 25-28, 2016, at the Boston Convention and Exhibition Center in Boston. The 2016 Annual Meeting is expected to attract more than 11,000 attendees from across the globe, including oncologists from all disciplines and members of the entire radiation oncology team. Led by ASTRO president David C. Beyer, MD, FASTRO, the 2016 meeting will feature keynote addresses from Kathleen Sebelius, former U.S. Secretary of Health and Human Services; Thomas James Lynch Jr., MD, Chair and CEO, Massachusetts General Physicians Organization; and Jason Ragogna, general manager, SMS and Safety Alliances, Corporate Safety, Security, and Compliance, Delta Air Lines, Inc. The Presidential Symposium, “Prostate Cancer: Defining Value and Delivering It,” highlights the meeting’s theme of “Enhancing Value, Improving Outcomes” and will feature recent practice-changing studies and current developments in value-based care for prostate cancer. ASTRO’s four-day scientific meeting will feature a record number of abstracts, including 368 oral presentations, 1,760 posters and 180 digital posters in more than 50 educational sessions and 20 scientific panels for 20 disease-site tracks. For more information about ASTRO’s 58th Annual Meeting, visit [www.astro.org/AnnualMeeting](http://www.astro.org/AnnualMeeting). For press registration and news briefing information for ASTRO’s 58th Annual Meeting, visit [www.astro.org/AMPress](http://www.astro.org/AMPress).*

**ABOUT ASTRO**

*ASTRO is the premier radiation oncology society in the world, with more than 10,000 members who are physicians, nurses, biologists, physicists, radiation therapists, dosimetrists and other health care professionals who specialize in treating patients with radiation therapies. As the leading organization in radiation oncology, the Society is dedicated to improving patient care through professional education and training, support for clinical practice and health policy standards, advancement of science and research, and advocacy. ASTRO publishes three medical journals, International Journal of Radiation Oncology • Biology • Physics ([www.redjournal.org](http://www.redjournal.org)), Practical Radiation Oncology ([www.practicalradonc.org](http://www.practicalradonc.org)) and Advances in Radiation Oncology ([www.advancesradonc.org](http://www.advancesradonc.org)); developed and maintains an extensive patient website, RT Answers ([www.rtanswers.org](http://www.rtanswers.org)); and created the Radiation Oncology Institute ([www.roinstitute.org](http://www.roinstitute.org)), a nonprofit foundation to support research and education efforts around the world*

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*that enhance and confirm the critical role of radiation therapy in improving cancer treatment. To learn more about ASTRO, visit [www.astro.org](http://www.astro.org).*

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**Extreme Hypofractionation vs. Conventionally Fractionated Radiotherapy for Intermediate Risk Prostate Cancer: Early Toxicity Results from the Scandinavian Randomized Phase III Trial "HYPO-RT-PC"**

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**Purpose/Objective(s):** Prostate cancer is postulated to have high radiation-fractionation sensitivity which suggests a potential therapeutic benefit for hypofractionated (HF) radiotherapy (RT). Results from randomized studies investigating efficacy and side-effects of *moderately* hypofractionated (M-HF) schedules have recently been reported in the literature. Data from randomized trials with *extreme* hypofractionation (E-HF) are however hitherto lacking. We here report two-year toxicity results from the Scandinavian multicenter phase III trial (HYPO-RT-PC) comparing E-HF with conventional fractionation (CF).

**Materials/Methods:** The HYPO-RT-PC non-inferiority trial accrued 1200 intermediate risk prostate cancer patients (T1c-T3a, PSA  $\leq 20$  with one or two of the following risk factors; T3a or Gleason  $\geq 7$  or PSA  $> 10$ ) from July 2005 to Nov. 2015. Patients were randomized with a 1:1 allocation ratio to either CF, 39x2.0 Gy=78 Gy over 8 weeks, or to E-HF, 7x6.1 Gy=42.7 Gy over 2.5 weeks (RT every other weekday). No androgen deprivation therapy was allowed. The two treatment schedules were designed to be equieffective for late normal tissue complication probability ( $\alpha/\beta=3$  Gy). Image guided RT based on fiducial markers was delivered to the prostate only (CTV) with a 7 mm isotropic CTV-PTV margin. The main OAR constraint was  $V_{90\%} \leq 15\%$  for rectum. A majority of the patients (80%) were treated with 3DCRT and the remaining with VMAT. Physician's evaluation of side-effects was performed according to a modified RTOG scale. Patient Reported Outcome Measurement (PROM) was performed with the PCSS questionnaire using a VAS scale to evaluate urinary and bowel symptoms as well as sexual function.

**Results:** Median follow-up time from randomization for the entire patient population is 4.2 years. 866 eligible patients had until May 2016 reached the two-year follow-up. There were no significant differences in the prevalence of physician reported grade 2+ toxicity at two years between E-HF and CF for urinary (5.4% vs. 4.6%,  $p=0.59$ ) and bowel (2.2% vs. 3.7%,  $p=0.20$ ) toxicity. The corresponding figures for acute toxicity at end of RT was 27.6% vs. 22.8% ( $p=0.11$ ) and 9.4% vs. 5.3% ( $p=0.023$ ), respectively. Impotence at two years was 34% in both arms compared to 16% at baseline. PROM data revealed no significant differences in any of the individual items/questions at two years. A small, but significant worse urinary function was observed in the the E-HF arm compared to CF in 4/14 symptoms at one year. At end of RT, bowel function had significantly worse PROM scores in the E-HF arm in 7/10 items but no significant differences at 3 and 6 months. Sexual function was similar in both arms.

**Conclusion:** E-HF resulted in a low incidence of side-effects with no significant differences compared to CF at the two-year follow-up.

Clinical trial information: ISRCTN45905321.