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

A. Widmark¹, A. Gunnlaugsson², L. Beckman³, C. Thellenberg-Karlsson¹, M. Hoyer⁴, M. Lagerlund⁵, P. Fransson⁶, J. Kindblom⁷, C. Ginman⁸, B. Johansson⁹, M. Seke¹⁰, K. Björnlinger¹¹, E. Kjellén², L. Franzen¹, and P. Nilsson²

¹Department of Radiation Sciences, Oncology, Umeå University, Umeå, Sweden, ²Department of Oncology and Radiation Physics, Skåne University Hospital, Lund University, Lund, Sweden, ³Department of Oncology, Sundsvall Hospital, Sundsvall, Sweden, ⁴Department of Oncology, Aarhus University Hospital, Aarhus, Denmark, ⁵Kalmar Hospital, Kalmar, Sweden, ⁶Department of Nursing, Umeå University, Umeå, Sweden, ⁷Department of Oncology, Institute of Clinical Sciences, The Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, ⁸Department of Oncology, Karlstad Central Hospital, Karlstad, Sweden, ⁹Department of Oncology, Örebro University Hospital, Örebro University, Örebro, Sweden, ¹⁰Centrallasarettet Växjö, Växjö, Sweden, ¹¹Ryhov Hospital, Jönköping, Sweden
Background

• Prostate cancer is postulated to have high radiation-fractionation sensitivity ➔ 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 (CHHiP, HYPRO, RTOG 0415)

• Data from randomized trials with extreme hypofractionation (E-HF) are lacking at this point, however
Patients and Method

• Open randomized phase III trial
  – Non-inferiority design
  – 1200 patients accrued
    • July 2005-Nov 2015
  – Intermediate risk PCa
    • T1c-T3a, PSA ≤ 20, GI ≥ 7,
      1-2 of these risk factors were required
  - No androgen deprivation therapy as allowed

Conventional fractionation (CF):
39*2.00 Gy = 78.0 Gy over 8 weeks

Extreme hypofractionation (E-HF):
7*6.10 Gy = 42.7 Gy over 2.5 weeks

- Equieffective for late normal tissue complication probability
  (α/β=3 Gy)
Radiation Therapy

• IGRT based 3D-CRT or VMAT/IMRT

90% (80%) 3D-CRT

10% (20%) VMAT
Results: Physician’s evaluation

Urinary toxicity ≥ grade 2

Bowel toxicity ≥ grade 2

Physician's evaluation
Results: Patient-reported outcome measurements (PROM)

"Do you have problems with your urinary tract?"

"Do you have problems with your bowel?"
Results: Patient-reported outcome measurements (PROM)

“Do you have a problem with your sex life?”

![Graph showing symptom severity over time for CF and E-HF groups. The graph includes data points for pre RT, RT end, 3m, 6m, 12m, and 24m. The x-axis represents time in months, and the y-axis represents symptom severity. The p-value is 0.71.]

- n (CF) = 316, n (E-HF) = 319
- n (CF) = 283, n (E-HF) = 270
- n (CF) = 265, n (E-HF) = 280
- n (CF) = 281, n (E-HF) = 286
- n (CF) = 281, n (E-HF) = 293
- n (CF) = 294, n (E-HF) = 284
Conclusions

• Extreme hypofractionation resulted in a low incidence of side-effects with no significant differences compared to conventional fractionation at two years

• Evaluation of primary endpoint due in approximately one year