LBA259

Oral Abstract Session

Long-term results of dose escalation (80 vs 70 Gy) combined with long-term androgen deprivation in high-risk prostate cancers: GETUG-AFU 18 randomized trial.

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Background: Radiotherapy (RT) delivered in combination with androgen deprivation therapy (ADT) improve survival for patients with prostate adenocarcinoma. RT given at a dose of 80 Gy is generally well tolerated but the occurrence of grade 3-4 toxicities is significantly more frequent than at a dose of 70 Gy. Furthermore, ADT has been reported to increase RT-related toxicity. Thus, we aimed to evaluate the efficacy and safety of dose escalation in combination with long term ADT in high-risk prostate cancer patients. **Methods:** The GETUG-AFU 18 study, sponsored by Unicancer, is a phase III randomized trial. Eligible patient had high-risk (cT3-T4 or PSA≥ 20 ng/ml or Gleason score ≥ 8-10) prostate adenocarcinoma with negative lymph-nodes status on CT-scan or MRI. Patients were randomly assigned to dose-escalated RT (80 Gy) or conventional-dose (70 Gy) with 3 years of ADT in both arms. Randomization (1:1) was stratified on pelvic lymph-nodes dissection (PLND; yes or no) and institution. Pelvic nodal irradiation (46 Gy) was performed for all patients except in case of negative PLND. The primary endpoint is the biochemical or clinical progression-free survival (bcPFS) at 5 years following ASTRO-Phoenix definition. Secondary endpoints are overall survival (OS), acute and late toxicity (CTCAE v3), and quality of life. To improve bcPFS from 65 to 75% (Hazard Ratios [HR] = 0.67), 500 patients were required (a= 5% and 1-b= 80%) with 197 events at 5 years. **Results:** 505 patients were included between June 2009 and January 2013. Main characteristics of the population were median age of 70.6 years (range 52-80); 268 (53.1%) patients with a Gleason score ≥ 8; median PSA value of 13.8 ng/ml (0.4-109.9); 62.3% of patient with cT3, and 16.4% with PLND. There was no imbalance between groups for major prognostic factors. The bcPFS was significantly improved in the dose-escalated RT arm compared with conventional RT arm (HR = 0.56, [95% CI, 0.40-0.76], p = 0.0005). The 5-year bcPFS was 91.4% (95% CI, 87.0-94.4) and 88.1% (95% CI, 83.2-91.6), and the 7-year bcPFS 88.1% (95% CI, 83.1-91.7) and 79.2% (95% CI, 73.1-84.0) in dose-escalated RT and conventional RT, respectively. We did observe significant differences in prostate cancer-specific survival (HR = 0.48 [95% CI, 0.27-0.83], p = 0.0090) and overall survival (HR = 0.61 [95% CI, 0.44-0.85], p = 0.0039). No prognostic factors were identified for bcPFS. Regarding late toxicities, there was no significant difference between arms with 78.2% and 76.1% of ≥Grade 2 toxicity with dose-escalated RT and conventional RT, respectively. **Conclusions:** Dose-escalation RT in combination with long-term ADT is effective and safe, increasing not only the bcPFS rate but also specific survival and overall survival in high-risk prostate cancer patients without increasing long-term toxicity. Clinical trial information: NCT00967863. Research Sponsor: French National Cancer Institute; French National Cancer League; AstraZeneca.