Highlights From the 2016 American Society of Clinical Oncology Genitourinary Cancers Symposium

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Hypofractionated High-Dose Intensity-Modulated Radiotherapy in Prostate Cancer

The phase 3 CHHiP (Conventional or Hypofractionated High Dose Intensity Modulated Radiotherapy in Prostate Cancer) trial compared 2 different schedules of hypofractionated, high-dose, intensity-modulated radiotherapy against standard radiotherapy in patients with localized prostate cancer. The standard radiotherapy schedule was 37 fractions (f) of 2 Gy to a total of 74 Gy. The hypofractionated schedules were 3 Gy treatments given in either 20 f to a total of 60 Gy or 19 f to a total of 57 Gy. More than 3000 patients were included in the study. Most patients (73%) were at intermediate risk. A previous analysis was presented at the 2015 European Cancer Congress (ECC).

Event-free survival at 5 years was 90.6% for the 60 Gy/20 f arm, 88.3% for the 74 Gy/37 f arm, and 85.9% for the 57 Gy/19 f arm. The study met its main primary endpoint by showing that 60 Gy/20 f was noninferior to 74 Gy/37. The study did not show clear noninferiority of the 57 Gy/19 f arm vs the 74 Gy/37 f arm. The improvement of 60 Gy/20 f over 57 Gy/19 f was statistically significant. Acute bowel toxicity was significantly higher in the hypofractionated groups than in the control group. There was a small increase in late bowel toxicities with 60 Gy/20 f as compared with 57 Gy/19 f.

Dearnaley DP, Syndikus I, Mossop H, et al. Comparison of hypofractionated high-dose intensity-modulated radiotherapy schedules for prostate cancer: results from the phase III randomized CHHiP trial (CRUK/06/016) [ASCO GU abstract 02]. *J Clin Oncol*. 2015;33(suppl).

Follow-up Analysis of the METEOR Trial Confirms Benefit With Cabozantinib in Renal Cell Carcinoma

The phase 3 METEOR (A Study of Cabozantinib [XL184] vs Everolimus in Subjects With Metastatic Renal Cell Carcinoma) trial compared cabozantinib (Cometriq, Exelixis) vs everolimus (Afinitor, Novartis), the standard of care, in patients with progressive, advanced renal cell carcinoma. In an initial analysis presented at the 2015 ECC of the first 375 patients, progression-free survival (PFS) was nearly doubled in the cabozantinib arm compared with the everolimus arm, at 7.4 months vs 3.8 months (hazard ratio [HR], 0.58; 95% CI, 0.45-0.75).

At the 2016 American Society of Clinical Oncology Genitourinary Cancers (ASCO GU) meeting, Bernard Escudier, MD, provided updated PFS data for the entire intent-to-treat cohort (N=658), as well as other outcome data and results from a prespecified subgroup analysis. The median PFS was 7.4 months for the cabozantinib arm vs 3.9 months for the everolimus arm (HR, 0.52; 95% CI, 0.43-0.64; $P<.001$). Cabozantinib maintained an improvement over everolimus regardless of the patient's risk status, disease burden, sites of metastases, or previous treatments. Tumor shrinkage occurred in 75% of the cabozantinib arm vs 48% of the everolimus arm.

Cabozantinib was associated with more grade 3/4 adverse events than everolimus (68% vs 58%). The most common grade 3/4 adverse events seen with cabozantinib were hypertension (15%), diarrhea (11%), and fatigue (9%).

Escudier BJ, Motzer RJ, Powles T, et al. Subgroup analyses of METEOR, a randomized phase 3 trial of cabozantinib versus everolimus in patients (pts) with advanced renal cell carcinoma (RCC) [ASCO GU abstract 499]. *J Clin Oncol*. 2015;33(suppl).

Early Findings From the ERADICATE Trial in Prostate Cancer

The open-label, prospective, phase 2 ERADICATE (Open Label Phase Two Trial of Radium Ra 223 Dichloride With Concurrent Administration of Abiraterone Acetate Plus Prednisone in Symptomatic Castration-Resistant [Hormone-Refractory] Prostate Cancer Subjects With Bone Metastasis) trial is evaluating the efficacy of concurrent administration of radium-223 and abiraterone acetate (Zytiga, Janssen) in men with castration-resistant prostate cancer and symptomatic bone metastases. The trial has enrolled 36 patients. Information regarding quality of life and bone pain was gathered at study enrollment and then again after the final treatment cycle.

Neal Shore, MD, presented interim results for the 30 patients who have received all 6 cycles of therapy. The patients reported a decrease in bone pain overall, as well as in bone pain that interfered with work, general activity, and mood. They also reported significant improvements in quality of life, with decreased pain, less life interference from their disease, and improved sleep quality. Data regarding efficacy and other outcomes are forthcoming.

Shore ND, Tutrone RF, Mariados NF, Nordquist LT, Mehlhaff BA, Harrelson SS. Interim results from eRADicAte: an open-label phase 2 study of radium Ra 223 dichloride with concurrent administration of abiraterone acetate plus prednisone in castration-resistant prostate cancer subjects with symptomatic bone metastases [ASCO GU abstract 177]. *J Clin Oncol*. 2015;33(suppl).

Gemcitabine, Cisplatin, and Ipilimumab for Metastatic Urothelial Cancer

A phase 2 trial examined the use of gemcitabine (Gemzar, Lilly), cisplatin, and ipilimumab (Yervoy, Bristol-Myers Squibb) in metastatic urothelial cancer. The trial enrolled 36 patients and used a phased treatment schedule. Patients received 2 cycles of gemcitabine plus cisplatin alone followed by 4 cycles of gemcitabine, cisplatin, and ipilimumab.

The objective response rate was 64%, with 50% partial responses and 14% complete responses. At the time of the data analysis, 64% of the patients had died. The median survival was 14.6 months. The 1-year overall survival was 59%, with a lower bound of the 90% CI of 41%. The study therefore did not meet its primary endpoint, which was a lower bound of the 90% CI exceeding 60%.

Most adverse events were grade 1/2, but 72% of patients experienced at least 1 grade 3/4 adverse event. Most grade 3/4 adverse events were hematologic. Nonhematologic toxicities were consistent with immune-related therapies, and included diarrhea and colitis.

Galsky MD, Hahn NM, Albany C, et al. Phase II trial of gemcitabine + cisplatin + ipilimumab in patients with metastatic urothelial cancer [ASCO GU abstract 357]. *J Clin Oncol*. 2015;33(suppl).

Bipolar Androgen Therapy in Prostate Cancer

Michael Schweizer, MD, presented results for a single-arm, open-label, phase 2 trial evaluating a treatment regimen that alternated androgen-deprivation therapy with bipolar androgen therapy in men with hormone-sensitive prostate cancer. The 33 enrolled patients first received treatment with 6 months of androgen-deprivation therapy. At the end of this treatment, patients with a prostate-specific antigen (PSA) below 4 ng/mL (or ≥50% below baseline) went on to receive 2 rounds of androgen-deprivation therapy alternating with bipolar androgen therapy. These rounds consisted of 3 cycles of bipolar androgen therapy and 12 weeks of androgen-deprivation therapy alone. The primary endpoint was the percentage of patients with a PSA below 4 ng/mL by study end. Among the 33 enrolled patients, 29 received bipolar androgen therapy.

The primary endpoint was met, with 59% of patients achieving a PSA below 4 ng/mL by the study's end. An undetectable PSA (<0.2 ng/mL) was reported in 10% of patients. In all 26 patients who completed the study as designed, PSA decreased compared with the baseline assessment. Quality of life was improved after the first round of bipolar androgen therapy.

Schweizer MT, Wang H, Luber B, et al. Bipolar androgen therapy (BAT) in men with hormone sensitive (HS) prostate cancer (PC) [ASCO GU abstract 236]. *J Clin Oncol*. 2015;33(suppl).

The Impact of Aspirin on Mortality in Prostate Cancer

In a large observational study, regular use of aspirin decreased mortality from prostate cancer. The study gathered data from a population of 22,071 male physicians with 27 years of follow-up. There were 3193 diagnoses of prostate cancer, and 403 men died of the disease. Regular aspirin use was defined as an average weekly intake exceeding 3 tablets.

A multivariate analysis showed that regular aspirin use was associated with decreased risk of lethal prostate cancer (HR, 0.76; 95% CI, 0.62-0.93). Regular aspirin use before the diagnosis of prostate cancer did not affect mortality. A borderline reduction in mortality was seen with regular aspirin use at the time of diagnosis (HR, 0.82; 95% CI, 0.67-1.00). After diagnosis, regular aspirin use was associated with a significant reduction in prostate cancer mortality (HR, 0.61; 95% CI, 0.47-0.78) and overall mortality (HR, 0.76; 95% CI, 0.65-0.89). Regular aspirin use did not correspond to the incidence of prostate cancer, whether for total cases, high-grade cases, or advanced cases.

Allard CB, Downer MK, Preston MA, et al. Regular aspirin use and the risk of lethal prostate cancer in the Physicians' Health Study [ASCO GU abstract 306]. *J Clin Oncol*. 2015;33(suppl).

Statin Use and the Treatment Duration of Abiraterone Acetate in Prostate Cancer

A retrospective review of men with castration-resistant prostate cancer aimed to determine whether statins compete with abiraterone for influx by SLCO2B1 and thereby diminish drug efficacy. The duration of treatment with abiraterone was used as a surrogate marker for time to progression. The study included 224 patients who were eligible for analysis. The median duration of abiraterone therapy was 10.7 months. At the time of data analysis, 71% of patients had discontinued abiraterone. The median follow-up from the abiraterone initiation was 27.8 months.

Contrary to the authors' initial hypothesis, there was a trend toward longer use of abiraterone among patients receiving statins. The relationship between statin use and abiraterone duration was not impacted by adjustment for previous use of docetaxel, enzalutamide (Xtandi, Astellas/Medivation), or site of metastases. There was a nonsignificant trend toward longer abiraterone duration in statin users, at 14.2 months vs 9.2 months (HR, 0.79; 95% CI, 0.57-1.09; P=.14). The previous use of docetaxel or enzalutamide was significantly associated with shorter abiraterone duration. In both cohorts, approximately 80% of patients experienced a decline in levels of PSA.

Harshman LC, Werner L, Nakabayashi M, et al. The impact of statin use on abiraterone acetate (AA) treatment duration in patients with castration-resistant prostate cancer (CRPC) [ASCO GU abstract 196]. *J Clin Oncol*. 2015;33(suppl).