Abstract for ESTRO 2019 study 301

Title:

First randomized study of Hafnium nanoparticles activated by radiotherapy in soft tissue sarcoma

Authors:

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Purpose/Objectives(s):

Preoperative radiotherapy (RT) is an option for a subset of patients with locally advanced primary or relapsed tumors. Yet, its impact on efficacy in terms of pathological response is limited, highlighting the need for novel multimodal therapies aimed at local control with low toxicity.

NBTXR3 is made of hafnium oxide nanoparticles which, injected intratumorally (IT) and activated by ionizing radiation, yield a tumor-localized high energy deposit and increase cell death compared to the same dose of RT alone.

We report here the results of a phase II/III randomized clinical trial of NBTXR3 given as preoperative treatment to patients with locally advanced soft tissue sarcoma (STS) of the extremity and trunk wall [NCT02379845].

Methods:

Act.In.Sarc is an international, multicenter, open-label, active-controlled phase II/III trial in which patients (pts) with locally advanced STS of the extremity or trunk wall were randomized 1:1 to receive a single IT NBTXR3 injection and RT (Arm A) or RT alone (Arm B), followed by surgical resection. RT consisted of Intensity Modulated RT or 3D-RT of 2Gy*25 fractions (total 50 Gy) over 5 weeks.

The primary endpoint was pathological Complete Response Rate (pCRR), defined as the proportion of pts presenting <5% of residual viable cancer cells evaluated by a Central Review Board on

anonymized tumor specimen. Key secondary endpoints included negative surgical margin (R0) and general safety.

Results:

Among the 180 randomized pts, 176 were included in the intent-to-treat full analysis set (ITT-FAS). In the ITT-FAS population, pCRR was 16.1% in Arm A vs 7.9% in Arm B (p=0.0448). R0 margin was achieved in 77.0% of pts in Arm A vs 64.0% in Arm B (p=0.0424). The limb amputation rate, another secondary outcome, was decreased by 50% in Arm A as compared to Arm B. NBTXR3 showed very good local tolerance without any modification of RT alone safety profile. In all the treated pts in Arm A, who received any amount of NBTXR3 or at least one RT dose, the IT administration of NBTXR3 caused injection-site pain in 12 (13.5%) pts. NBTXR3 was also associated with grade 3-4 acute immune reactions in 7 (7.9%) pts, but these adverse events were of short duration, manageable, and, in some cases, resolved spontaneously. Long-term efficacy and safety results will be presented.

Conclusion:

In this study both the primary and secondary endpoints (pCRR and R0 rate, respectively) were met with a safety profile of NBTXR3 activated by RT comparable to that of RT alone. As pCR is associated with improved progression-free and overall survival, NBTXR3 activated by RT represents a new preoperative treatment option for locally advanced STS. These data support ongoing studies investigating NBTXR3 in recurrent/metastatic HNSCC or metastatic non-small cell lung cancer [NCT03589339]; HNSCC [NCT01946867; NCT02901483]; prostate cancer [NCT02805894], liver cancer [NCT02721056] and rectal cancer [NCT02465593].