Consolidation with high dose chemotherapy for responding patients to standard chemotherapy in advanced, metastatic soft tissue sarcoma (STS). A randomized trial from FNCLCC- French Sarcoma Group

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Abstract:

Background:
Whether high dose (HD) chemotherapy improves disease-free (DFS) or overall (OS) survival has been suggested in phase II trial, but never explored in a randomized setting. This randomized, open, phase III study was designed to assess whether or not an HD chemotherapy with peripheral blood stem cells (PBSC) would improve OS in patients with advanced or metastatic STS responding to MAID chemotherapy.

Methods:
Pts aged 18 to 65 and with advanced STS were enrolled. After 4 courses of MAID, patients in PR or CR, or in whom complete surgical removal of all lesions was performed, were proposed for randomisation between 2 more cycles of MAID (control arm) vs 1 MAID followed by an intensification with MICE, ie: Mesna (3.6g/m2, d1-5), Ifosfamide (4g/m2, d1-4), Carboplatin (UCA5, d2-4) and Etoposide (300mg/m2, d1-4), followed by PBSC (HD arm). The primary endpoint was OS and the study was designed to detect by logrank test a 25% difference between the arms.

Results:
From 03/00 to 06/08, 266 patients were included and 87 were randomised (15 centres); low accrual and new treatment concepts lead to an IDMC in 11/08 who analysed 45 treated in the control arm (41 with full treatment) and 40 in the HD arm [only 21 received MICE, because consent withdrawal (6), insufficient PBSC harvest (5), tumor reprogression (4)]. Baseline characteristics (pts and tumors) were similar between treatment arms. With a 39 months follow-up, 25 pts were alive in the control arm, and 19 in the HD arm.
The 3yearsOS was 45.5% for control arm versus 35.8 for HD arm (HR = 1.12; 95% CI 0.58, 2.14; p = 0.72 Intention to treat analysis); PFS was 29.9% and 12.1 respectively (HR = 1.48; 95% CI 0.87, 2.53; p = 0.14). Higher rate of grade 3-4 hematologic (87% vs 46%), and digestive toxicity (33% vs 0%) were observed in the HD arm. Two treatment-related deaths occurred, both in the HD arm.

Conclusions: In this study, HD chemotherapy for STS patients didn't improve OS and DFS. Consolidations with new concepts have to be explored.