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ABSTRACT # 65

RANDOMIZED PHASE II TRIAL ON PRIMARY CHEMOTHERAPY (CHT) WITH HIGH-DOSE METHOTREXATE (MTX) ALONE OR ASSOCIATED WITH HIGH-DOSE CYTARABINE (ARAC) FOR PATIENTS (PTS) WITH PRIMARY CNS LYMPHOMA (PCNSL)

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Background

MTX-based CHT is the conventional approach to PCNSL, but superiority of polyCHT over MTX alone is unproven. A benefit of adding araC to MTX has been suggested by a meta-analysis and a large retrospective series.

Patients

PCNSL pts (HIV-; 18-75 ys; PS \leq 3; 2004-2007) were randomized to receive 4 courses (interval 3 weeks) of MTX 3.5 g/mq (arm M) or MTX (same dose) + araC 2 g/mq x 2/d, d 2-3 (arm MA). CHT was followed by radiotherapy (RT). Pts were stratified based on IELSG score and centre RT policy for pts >60 ys in complete remission (CR) after CHT. CR rate (CRR) after CHT was the primary endpoint; planned accrual (\pm 0.05 \pm 0.2) for P0 30% and P1 50% was 39 pts/arm.

Results

79 pts (median age 58 ys) were randomized to receive M (N=40) or MA (N=39). IELSG risk was low in 22 (28%) pts, intermediate in 48 (61%) and high in 9 (11%). Sixty-nine pts (87%) had a DLBCL. Ocular and meningeal disease were detected in 14% and 7% of cases, respectively. No differences in pts' characteristics between arms were observed. 231 (73%) of the 316 planned courses were actually delivered (M 71%; MA 76%). CHT was interrupted due to progressive disease in 20 (50%) M pts and 8 (21%) MA pts ($p<0.001$), toxicity in 1 (3%) M pt and 7 (18%) MA pts ($p=0.009$) and refusal in 2 MA pts. \geq 25% dose reduction was indicated in 1 M pt and 17 MA pts. G4 neutropenia (10% vs. 74%), G4 thrombocytopenia (5% vs. 64%) and infections (3% vs. 23%) were more common in MA arm. All G3-4 non-hematological toxicity rates were <5%. One M pt (3%, cardiotoxicity) and 3 MA pts (8%, sepsis - hepatotoxicity) died of toxicity. Response after CHT was CR in 7 M pts and 18 MA pts (CRR: 18% vs. 46%; $p=0.0002$) and partial in 10 M and 9 MA pts (ORR 43% vs. 69%; $p=0.0002$). After CHT-RT, 11 M pts and 25 MA pts achieved CR (28% vs. 64%; $p<0.0001$). At a median f-up of 16 mo, 29 M pts and 22 MA pts experienced failure (PD, relapse, death), with a 3-yr EFS of 24% vs. 35% ($p=0.02$).

Conclusion

This is the first randomized trial on PCNSL with completed accrual. The addition of araC to MTX was associated with significantly better outcome and acceptable toxicity. MTX+araC may be the control arm for future randomized trials.