LB2370 R-CODOX-M/R-IVAC VERSUS DOSE-ADJUSTED(DA)-EPOCH-R IN PATIENTS WITH NEWLY DIAGNOSED HIGH-RISK BURKITT LYMPHOMA; FIRST RESULTS OF A MULTI-CENTER RANDOMIZED HOVON/SAKK TRIAL.

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

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Background: Optimal first-line treatment for patients with high-risk Burkitt lymphoma (BL) remains to be defined. Treatment with high dose multi-agent chemotherapy such as R-CODOX-M/R-IVAC is effective (2 yr PFS 64-71%) at the cost of significant toxicity and long hospitalization. DA-EPOCH-R has demonstrated favorable 2 yr PFS of 85% and less toxicity in a phase II study. Here, we present the first results of a randomized trial comparing R-CODOX-M/R-IVAC with DA-EPOCH-R (EudraCT2013-004394-27).

Aims: The trial was designed to demonstrate an improvement of 2 yr PFS (primary endpoint) from 70% with R-CODOX-M/R-IVAC (arm A) to 85% with DA-EPOCH-R (arm B) in patients with newly diagnosed BL.

Methods: Patients (18-75 yr) with newly diagnosed (sporadic and HIV-associated), high-risk BL were eligible. High-risk was defined as any of: elevated LDH, WHO PS ≥ 2, stage III/IV, mass ≥ 10 cm. Central nervous system (CNS) involvement was excluded. After obtaining informed consent, patients were randomly assigned to treatment with 2 cycles of R-CODOX-M/R-IVAC or 6 cycles of DA-EPOCH-R. All patients received intrathecal CNS prophylaxis. EOT response was assessed by PET-CT scan. Complete Metabolic Remission (CMR) was defined as Deauville score 1-3. To confirm the hypothesis, 260 patients were needed. Due to slow accrual rate and the inability of another cooperative group to participate, the trial was closed prematurely. Data cut off for analysis was April 16, 2022.

Results: Between 2014 and 2021, 89 patients were enrolled. Five patients were excluded (3 CNS involvement, 2 no BL), 84 patients were randomized (n=43 arm A, n=41 arm B). Median follow-up is 19.1 (0.03-88.4) months. Baseline characteristics were well balanced between both arms (median age 50 yr (18-75) vs 56 yr (22-74), p=0.30), stage III/IV 88% vs 92% (p=0.62) in arm A and B respectively. Central pathology review was performed in 89% of patients. R-CODOX-M/R-IVAC was fully dosed in 92% of cycles (range 86-95% for different components). Maximum dose level (DL) of DA-EPOCH-R was DL1 in 35%, DL2 in 19%, DL3 in 24%, and DL4 in 22% of cycles of R-CODOX-M/R-IVAC or 6 cycles of DA-EPOCH-R. All patients received intrathecal CNS prophylaxis.
patients. In arm A 9/43 (21%) patients discontinued treatment (reason: 4 excessive toxicity, 3 progression, 1 refusal, 2 death (1 BL, 1 sepsis)) vs 4/41 (10%, reason: none excessive toxicity, 3 progression, 1 death (COVID)) in arm B. All other patients completed planned treatment. In arm A 28/43 (65%) patients achieved CMR and in arm B 27/41 (66%). In arm A 34/43 patients (79%) experienced AE grade (G) 3-5 (one G5: sepsis) and 30 SAE were reported in 21 patients, vs 30/41 (73%) patients with AE G3-5 (one G5: COVID) and 28 SAE in 20 patients in arm B. Most common SAE were infectious complications (infections and febrile neutropenia), 22/30 SAE (73%) in arm A vs 13/28 SAE (46%) in arm B (p=0.04). In arm A patients received a median of 2 (0-37) platelet transfusions and 5 (0-28) red blood cell transfusions vs 0 (0-6) and 1 (0-17) in arm B (p<0.01 for both). In arm A patients were hospitalized 46 nights (mean, 1-99) vs 25 nights (4-78) in arm B (p<0.01). Preliminary survival analysis demonstrated comparable estimated 2 yr OS rates of 75% in arm A and 76% in arm B. Causes of death were refractory/relapsed BL in 8 and 7 patients (arm A and B respectively), see Figure 1.

Summary/Conclusion: This is the first multi-center randomized trial comparing two different chemotherapy regimens in BL. The trial was closed prematurely. Treatment with DA-EPOCH-R resulted in comparable CMR and survival rates as R-CODOX-M/R-IVAC, but was associated with significant less infectious complications, transfusions and hospitalization days.