P1217 INTRATHECAL METHOTREXATE PROPHYLAXIS AND CENTRAL NERVOUS SYSTEM RELAPSE IN PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA TREATED WITH INTENSIFIED R-ACVBP STRATEGY

Topic: 19. Aggressive Non-Hodgkin lymphoma - Clinical

Loïc Renaud¹,², Pierre Stéphan³, sixte durand⁴, Guillaume Escure⁵, morschauser Franck⁶, vincent camus⁴, Hervé tilly⁴, Olivier casasnovas³, Sylvie Chevrel⁷, Catherine Thieblemont¹,²

¹Hemato-oncologie, DMU DHI;²Université de Paris, AP-HP, Hôpital Saint-Louis, F-75010 Paris, France;³Department of Hematology, University Hospital F. Mitterand and Inserm UMR 1231, Dijon, France;⁴Department of Hematology, Centre Henri Becquerel, University of Rouen, Rouen, France;⁵Department of Hematology, CHU Lille, Université de Lille 2, Lille, France;⁶Department of Hematology, CHU Lille, Unité GRITA, Université de Lille 2, Lille, France;⁷Biostatistiques, AP-HP, Hôpital Saint-Louis, Université de Paris – Paris Diderot, paris, France

Background:

Central nervous system (CNS) relapse of diffuse large B-cell lymphoma is relatively uncommon (2-5%) and remains catastrophic with a median survival of 2 to 5 months. Intrathecal (IT) or intravenous high-dose methotrexate (HD MTX) have limited if any prophylactic impact on CNS relapse. We recently demonstrated in a cohort of 2203 patients included in multicenter clinical trials conducted by LYSA and GLA/DSHNHL, that only 4 (1.6%) CNS relapses were seen with the R-ACVBP strategy in pts with aIPI 2, 3 (and intermediate/high CNS-IPI), while 15 (3.9%) relapses did occur after R-(Mega)CHO(E)P.

Aims: To address the role of IT in this intensified strategy R-ACVBP, we took the advantage of real world data of patients treated in four centers, and compared CNS relapses occurring in patients treated with R-ACVBP strategy with or without IT.

Methods: The LYSA R-ACVBP strategy include four cycles of R-ACVBP (75 mg/m² doxorubicin, and 1200 mg/m² cyclophosphamide; 2 mg/m² vindesine and 10 mg bleomycin on days 1 and 5) with four IT, two cycles of high dose methotrexate (3g/m²), four cycles of R-etoposide (300 mg/m²) and ifosfamide (1500 mg/m²) and 2 cycles of cytarabine(100 mg/m²) given sub cutaneously for 4 days. 233 patients with previously untreated diffuse large B-cell lymphoma (DLBCL) aged 18 to 59 years old received this intensified strategy between 2010 and 2020. We excluded 30 patients who received ASCT in first line and 10 others who received less than four cycles of R-ACVBP. We assessed the risk for of relapse and CNS-relapse. We also assessed the impact of the 2 courses of subcutaneous aracytine on overall survival (OS) and progression free survival (PFS).

Results:

A total of 193 pts were included. Median age was 44.4 years (IQR, 30.8-53, range: 17-62). Distribution of CNS IPI was not significantly different comparing IT (n=132) vs non-IT (n=61) groups within aIPI categories (Table 1). 92 patients did not receive the two courses of subcutaneous Aracytine (no AraC group) for consolidation and 101 patients received the two courses (AraC group).

With a median follow-up at 57.2 months, the 3 year OS and 3 year PFS of the whole cohort was 93.6% and 86.2%, respectively, without significant difference between IT and non IT groups in terms of OS (3yr-OS, 92.3% versus 95.1%, HR= 1.29 (95%CI, 0.41 to 4.04, p=0.67) and PFS (3yr-PFS, 84.4% versus 90.1%, HR= 1.26 (95%CI, 0.59 to 2.72, p=0.55).

The 3y-cumulative incidence of CNS relapse for pts treated IT group was 3.2% (95%CI, 1.0 to 7.4), and 3.3% (95%CI, 0.6 to 10.2) in the non-IT group (p= 0.93). In pts with aIPI 1, two patients experienced a CNS relapse, one in the IT group and one in the non-IT group. In pts with aIPI 2,3 and intermediate/high CNS IPI, 4 patients...
experienced a CNS relapse, three out of four in the IT group.

92 patients did not receive the two courses of subcutaneous Aracytine (no AraC group) for consolidation and 101 patients received the two courses (AraC group). Receiving or not AraC did not have any impact on the CNS relapse with a risk of CNS relapse at 4.1% (95% CI, 1.3 to 9.5) for patients receiving AraC and 2.2% (95% CI, 0.4 to 6.9) for patients not receiving AraC (p = 0.48).

**Summary/Conclusion:**

CNS relapse was rare in younger DLBCL treated with this intensified strategy. Only 6 CNS relapses were observed without difference between IT and non-IT groups. The results presented at the EHA will included the total cohort of more than 600 patients.

**Table 1. Distribution of the CNS-IPI according to the IT / non-IT groups.**

| CNS IPI groups | n=76 | n=127 | n=40 | n=63 | n=34 |
|----------------|------|-------|------|------|------|
| IT             |      |       |      |      |      |
| Non-IT         | IT   | Non-IT| IT   | Non-IT|     |
| 1 - low risk   | 39   | 21    | 0    | 0    |      |
| 2.3 - int risk | 19   | 6     | 66   | 28   |      |
| 4.5 - high risk| 0    | 0     | 17   | 6    |      |

**Abstract Book Citations:** Authors, Title, HemaSphere, 2022;6:(S3):pages. The individual abstract DOIs can be found at https://journals.lww.com/hemasphere/pages/default.aspx.

**Disclaimer:** Articles published in the journal HemaSphere exclusively reflect the opinions of the authors. The authors are responsible for all content in their abstracts including accuracy of the facts, statements, citing resources, etc.