globally, with high potential to shape the way of future drug development.

Keyword: molecular targeted therapies

No conflicts of interests pertinent to the abstract.

078 | NEW TRENDS IN LYMPHOMA TREATMENT IN WESTERN COUNTRIES

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Immunotherapy with chimeric antigen receptor (CAR) T-cells and bispecific antibodies undoubtedly represent the most advanced frontier in the treatment of lymphomas in Europe and North America. Real world experiences with CAR T-cells both in the United States and at some European institutions have replicated the favourable outcomes of pivotal clinical trials, with the achievement of objective response rates of 45%–55% in patients with diffuse large B-cell lymphoma treated beyond the second line, and yielding 2-year progression-free survival rates of 30%–45%. Importantly, at least 50% of the patients treated on a routine basis would have not qualified for a clinical trial, thus underscoring that CAR T-cells may represent a valuable option for a wide spectrum of patients who have failed chemotherapy and appear ineligible for autologous transplantation because of age or disease status.

Bispecific antibodies realize a T-cell-based immunotherapy in aggressive and indolent B-cell lymphomas: glofitamab, epcoritamab and odronextamab are now being extensively applied in the aggressive lymphoma setting, while mosunetuzumab is mainly given in patients with follicular lymphoma. Results in both aggressive and indolent lymphomas that substantially overlap with those of CAR T-cells along with a more favourable toxicity profile in terms of cytokine release syndrome and neurologic events, make bispecific antibodies an attractive option for multiply treated patients.

Given the experience gained with these agents, CAR T-cells are now being explored as first salvage and frontline treatment in aggressive lymphomas. Trials with bispecific antibodies combined with chemotherapy or targeted agents in less pretreated or untreated patients are ongoing.

Keywords: aggressive B-cell non-Hodgkin lymphoma, aggressive T-cell non-Hodgkin lymphoma, molecular targeted therapies immunotherapy

No conflicts of interests pertinent to the abstract.

SESSION 13 - FOLLICULAR LYMPHOMA

079 | A "FUNCTIONAL CURE" MAY BE ACHIEVABLE IN A SUBSET OF PATIENTS WITH FOLLICULAR LYMPHOMA TREATED WITH CHEMOIMMUNOTHERAPY: 15-YEAR FOLLOW-UP OF PHASE III SWOG-S0016

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Background: Follicular lymphoma (FL) is considered incurable with current therapies which include chemoimmunotherapy as the standard of care for first line. S0016 enrolled patients with untreated advanced FL (bulky stage II or III–IV) between 2001 and 2008 and randomized them to CHOP × 6 followed by (131) I-tositumomab radioimmunotherapy (CHOP-RIT) or CHOP-R × 6; no maintenance was included.

Methods: Fifteen-year PFS and OS were estimated according to the Kaplan–Meier method. Cumulative incidence of disease progression was calculated using the nonparametric Nelson-Aalen estimator with death without progression/relapse treated as a competing risk.

Results: Baseline characteristics between the CHOP-RIT (n = 267) and CHOP-R (n = 264) arms were balanced: age (median 53.4 vs. 54.5 years), B symptoms (26% vs. 29%), path grade 3 (9% vs. 8%), high FLIPI risk (26% vs. 22%), high β2M (55% vs. 53%), marrow involvement (55% vs. 56%) and bulky disease (26% vs. 24%).

After a median follow-up of 15.5 years, the 15-year OS was 70% (95% CI: 65.9%–74.1%) for the entire cohort, 67% (95% CI: 60.7%, 72.6%) for CHOP-RIT and 73% (95% CI: 67.2%, 78.4%) for the CHOP-R (p-value = 0.56) arm. The 15-year estimate of PFS for the entire cohort was 40% (95% CI: 36.0%, 44.7%). The PFS was superior in the CHOP-RIT arm [47% (95% CI: 40.4%, 53.0%)] versus CHOP-R [34% (95% CI: 28.2%, 40.0%)] (p-value = 0.004).

While the overall incidence of progression increased overtime, the average progression rate dramatically decreased: 6.8% (0–5 years), 2.3% (5–10 years), 1.1% (10–15 years) and 0.6% (15%–20%). Cumulative incidence of progression at 15-years for the entire study population was 50.5% (95% CI: 46.5%–54.8%) and was lower in the CHOP-RIT arm vs. CHOP-R arm [42.3% (95% CI: 36.1–48.4%) vs. 58.6% (95% CI: 52.2%–64.4%); p-value = 0.0009]

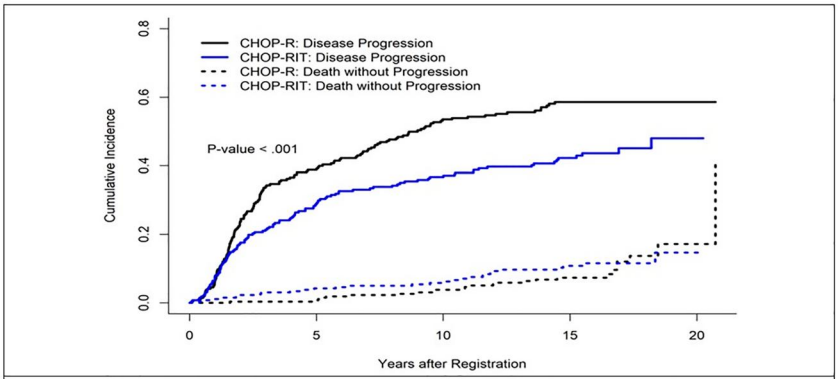

Figure: Cumulative incidence of disease progression and death without progression in both arms

There was no difference between the 2 arms in incidence of 2nd malignancies (19.7% vs. 22.1%; *p*-value = 0.52) or AML/MDS (5.3% vs. 2.2%; *p*-value = 0.08). The estimate of 15-year cumulative incidence of deaths due to 2nd malignancies were 7% and 5.4% in CHOP-RIT and CHOP-R arms (*p*-value = 0.45) but the 15-cumulative incidence of deaths due to AML/MDS was higher in CHOP-RIT arm (4.4% vs. 1.2%; *p*-value = 0.03). The most common causes of death were lymphoma (15.2%), 2nd malignancies (7.2%) and non-cancer medical issues (6.4%) in the CHOP-RIT arm and lymphoma (11.6%), non-cancer medical issues (8.6%) and 2nd malignancies (5.6%) in CHOP-R arm (*p*-value 0.27). The cumulative incidence of death without progression at 15-years was 9.1% (95% CI: 6.7%–11.9%).
Conclusion: With more than 15 years of follow-up, 40% of patients remain alive and progression-free after 6 cycles of CHOP-RIT or CHOP-R without maintenance therapy. The average rate of progression decreased overtime indicating a possibility of achieving a functional cure in a subset of patients. These results provide a benchmark for first-line studies utilizing novel agents.

The research was funded by: NIH/NCI/NCTN grants U10CA180888, U10CA180819

Keywords: chemotherapy, combination therapies, indolent non-Hodgkin lymphoma

Conflicts of interests pertinent to the abstract

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Consultant or advisory role: AbbVie, Genentech, AstraZeneca, Pharmacyclics, BeiGene, BMS, MorphoSys/Incyte, Kite, Eli Lilly, Genmab, Mustang Bio, Janssen, Regeneron, ADC therapeutics, Fate Therapeutics and MEI Pharma
Research funding: Mustang Bio, BMS, Pharmacyclics, Genentech, AbbVie,TG Therapeutics, BeiGene, AstraZeneca, Genmab, MorphoSys/Incyte, Vincerx.

J. P. Leonard
Consultant or advisory role: Roche/Genentech
Research funding: Roche/Genentech

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Consultant or advisory role: Incyte, Kite, Morphosys/Incyte, ADCT, Acrotech, Merck, Karyopharm, Servier, Beigene, Cellectar, Janssen, SeaGen, Epizyme, I-Mab bio, Gilead, Genentech, Lilly, Caribou, Fresenius-Kabi
Research funding: Merck, I-Mab bio, IgM Bio, Takeda, Gilead, AstraZeneca, Agios, Janssen, BMS, SeaGen, Teva, Genmab

080 | SAKK 35/14 RANDOMIZED TRIAL OF RITUXIMAB WITH OR WITHOUT IBRUTINIB FOR UNTREATED PATIENTS WITH ADVANCED FOLLICULAR LYMPHOMA IN NEED OF THERAPY

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