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ORAL ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Long-Term Efficacy of a 6-Month Regimen of Rituximab and Lenalidomide in Follicular Lymphoma Patients in Need of First Therapy: Updated Analysis of the SAKK 35/10 Randomized Trial

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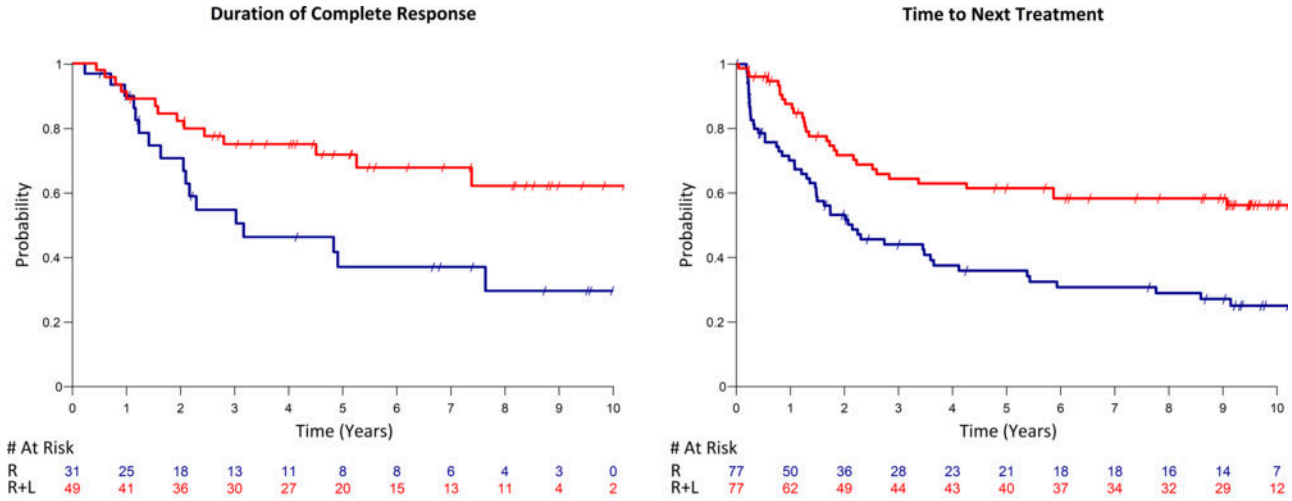
*Background:*The Swiss Group for Clinical Cancer Research (SAKK) and the Nordic Lymphoma Group (NLG) conducted the SAKK 35/10 randomized phase-2 trial (NCT0137605) to compare the effectiveness of rituximab (R) alone versus R combined with lenalidomide (L) as the initial treatment for symptomatic follicular lymphoma (FL). The primary endpoint analysis, which demonstrated higher complete remission (CR) rates with the combination therapy, was previously reported (Zucca et al. Blood 2019). This report provides a long-term analysis of time-to-event endpoints with a median follow-up of approximately 10 years. *Methods:*A total of 154 eligible patients with untreated grade 1 to 3a FL requiring systemic therapy were centrally randomized to receive either R monotherapy (375 mg/m2 IV on day 1 of weeks 1-4 and repeated during weeks 12-15 for responding patients) or R+L. In the combination arm, R was administered at the same schedule as the monotherapy, while L was taken

orally at a daily dose of 15 mg, starting 14 days before the first R administration, and continued until 14 days after the last R administration, for a total of 18 weeks. Random assignment to treatment arms was stratified based on histological grade (1-2 vs 3a), bulky disease (<6 vs ≥6 cm), Follicular Lymphoma International Prognostic Index (FLIPI) score (1-2 vs ≥3), and centre, using the minimization method.
The sample size was determined to detect a 20% increase in the CR/CRu rate with 90% power, using a one-sided Z-test with a false positive rate of 10% to compare the two treatment arms. The assessed endpoints, including progression-free survival (PFS), time to next anti-lymphoma treatment (TTNT), duration of CR/CRu (DoR), and overall survival (OS), were defined according to NCI international standardized criteria (Cheson et al. J Clin Oncol 1999).
*Results:*Seventy-seven patients (median age 63 years, 52% with stage IV and 47% with poor-risk FLIPI score) were assigned to the single-agent rituximab arm, and 77 patients (median age 61 years, 48% with stage IV and 47% with poor-risk FLIPI score) were assigned to the combination arm. The results for the primary endpoint were consistent with the positive initial analysis. At a median follow-up of 9.5 years, the overall survival was similar in both arms (77% vs. 78% at 10 years, p=0.881). However, significant, and sustained improvements were seen in all other time-to-event endpoints. Patients in the R+L arm had a longer PFS (median, 9.3 vs. 2.3 years; HR=0.58, 95% CI: 0.37-0.89; p=0.013) and TTNT (median, not reached vs. 2.1 years; HR=0.43, 95% CI: 0.27-0.67; p<0.001). DoR with R+L was also longer (median not reached vs 3.2 years with R only; HR=0.42, 95% CI: 0.21-0.86; p=0.014) and with over 60% of responders still in first remission at 10 years. The improved outcomes with R+L were not associated with unexpected toxicity. Grade ≥3 adverse events were more common with the combination regimen (56% vs. 22% of patients), with grade 3-4 neutropenia in 23% of patients receiving R+L and in 7% of those receiving R alone. Fatigue, diarrhea, and skin rash were more frequent with R+L, but mostly of grade 1-2 (grade 3 occurred in ≤ 5% in both arms, and no grade 4 was reported). The side effects were manageable, and there were no treatment-related deaths in either arm. Two cases of biopsy-proven into diffuse large B-cell lymphoma were reported in the R+L arm, and two cases of Hodgkin lymphoma were described in the R arm. Although their causal relationship with treatment is not completely clear, the number of second solid cancers was significantly higher in the R+L arm. Two cases of prostate cancer, two lung adenocarcinomas (one in situ), one small cell lung carcinoma, one rectal cancer, and four skin cancers (three squamous cell and one basal cell), were observed in the R+L arm, while only one solid tumor (prostate cancer) occurred in the R arm (p=0.09). Only one patient died of a second solid cancer (small cell lung carcinoma in the R+L arm). The rate of POD24 was 29% in the R+L arm vs. 34% in the R-arm (p=0.483).
*Conclusions:*The long-term results of the SAKK 35/10 trial demonstrated a durable benefit for the R+L combination compared to R alone. Notably, the adopted R+L schedule is considerably shorter than the standard R2 regimen (18 vs. 120 weeks). This provides a promising alternative when treatment is required but durable immunosuppression is undesirable.

Disclosures Zucca: *AstraZeneca:* Research Funding; *Curis:* Membership on an entity's Board of Directors or advisory committees; *Eli/Lilly:* Membership on an entity's Board of Directors or advisory committees; *Merck:* Membership on an entity's Board of Directors or advisory committees; *Miltenyi Biomedicine:* Membership on an entity's Board of Directors or advisory committees; *Roche:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Kite, A Gilead Company:* Other: travel grant; *BeiGene:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Celgene/BMS:* Research Funding; *BMS:* Membership on an entity's Board of Directors or advisory committees; *Incyte:* Membership on an entity's Board of Directors or advisory committees, Research Funding; *Ipsen:* Membership on an entity's Board of Directors or advisory committees; *Janssen:* Membership on an entity's Board of Directors or advisory committees, Research Funding. **Wahlin:** *Genmab:* Current holder of *stock options* in a privately-held company; *Roche:* Consultancy, Research Funding; *Gilead Sciences:* Research Funding. **Brown:** *Gilead:* Other: Advisory Board; *Roche:* Other: Advisory Board. **Ferreri:** *Gilead, Incyte, Novartis, PentixaPharm, Roche:* Consultancy; *Adienne:* Speakers Bureau; *ADC Therapeutics, Amgen, BeiGene, BMS, Genmab, Gilead, Hutchison Medipharma, Novartis, Pharmacyclics, PentixaPharm, Pfizer, Roche:* Research Funding; *Ospedale San Raffaele srl.:* Patents & Royalties. **Novak:** *Gilead:* Other: Advisory Boards; *BMS:* Other: Advisory Board; *Novartis:* Other: Advisory Boards. **Stathis:** *Merck/MSD:* Research Funding; *Loxo Oncology:* Research Funding; *Cellestia:* Research Funding; *Amgen:* Research Funding; *ADC Therapeutics:* Research Funding; *AbbVie:* Research Funding; *Janssen:* Consultancy; *Incyte:* Other: travel grant, Research Funding; *Eli Lilly and Company:* Consultancy; *Bayer:* Consultancy, Research Funding; *AstraZeneca:* Other: travel grant, Research Funding; *Novartis:* Research Funding; *Pfizer:* Research Funding; *Philogen:* Research Funding; *Roche:* Consultancy, Research Funding.

OffLabel Disclosure: Not registered schedule of the rituximab plus lenalidomide combination in patients with untreated follicular lymphoma



Long-Term Results of the SAKK 35/10 Randomized Trial of Rituximab Vs. Rituximab and Lenalidomide in Follicular Lymphoma in Need of First Therapy

Figure 1

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