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POSTER ABSTRACTS

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

Real World Results of Brexucabtagene Autoleucel for Patients with Relapsed/Refractory Mantle Cell Lymphoma - First German/Swiss Analysis

Georg Hess[1], *Vladan Vucinic*[2], *Kai Rejeski, MD*[3], *Enver Aydilek*[4], *Linda Simon, MD*[5], *Olaf Penack, MD*[6], *Christian Koenecke, MD*[7], *Malte von Bonin, MD*[8], *Bastian von Tresckow, MD*[9], *Martin Fehr, MD*[10], *Christiane Pott*[11], *Stephan Stilgenbauer, MD*[12], *Corinna Leng, MD PhD*[13], *Roland Schroers, MD*[14], *Johannes Duell, MD*[15], *Reinhard Marks, MD*[16], *Fabian Mueller, MD*[17], *Uta Brunnberg, MD*[18], *Andrea Kerkhoff, MD*[19], *Anke Ohler*[5], *Eva-Maria Wagner Drouet*[20], *Irene Schmidtmann*[21], *Matthias Theobald, MD*[20], *Martin Dreyling, MD*[22], *Peter Dreger, MD*[23]

[1] University Clinic Mainz, Mainz, Germany
[2] Department of Hematology, Cellular Therapy, Hemostaseology and Infectious Diseases, University of Leipzig, Leipzig, Germany
[3] University of Munich, LMU, Munich, Germany
[4] Universtity of Goettingen, Goettingen, Germany
[5] University Medical School of the Johannes Gutenberg-University, Mainz, Germany
[6] Department of Hematology, Oncology, and Cancer Immunology, Charité Universitätsmedizin Berlin, Campus Virchow Klinik, Berlin, Germany
[7] Department of Hematology, Hemostasis, Oncology, and Stem Cell Transplantation, Hannover Medical School, Hannover, Germany
[8] Department of Internal Medicine I, University Hospital, TU Dresden, Dresden, Germany
[9] Cancer Center Cologne Essen (CCCE), Cologne / Essen, Germany
[10] Division of Oncology and Hematology, Cantonal Hospital St. Gallen, St. Gallen, Switzerland
[11] Second Medical Department, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany
[12] Department of Internal Medicine III, Division of CLL, Ulm University, Ulm, Germany
[13] Charité, Berlin, DEU
[14] Knappschaftskrankenhaus Bochum, University Hospital Bochum, Bochum, Germany, Bochum, Germany
[15] Department of Internal Medicine II, Hematology and Oncology, University Hospital Wuerzburg, Wuerzburg, Germany
[16] Department of Hematology, Oncology and Stem Cell Transplantation, Faculty of Medicine, University of Freiburg, Freiburg, Germany
[17] Department of Internal Medicine 5, Hematology and Oncology, Friedrich-Alexander University of Erlangen-Nuremberg, Erlangen, Germany
[18] University of Frankfurt, Frankfurt, DEU
[19] Medical Department A for Hematology, Oncology, and Pneumology, University Hospital Muenster, Muenster, Germany
[20] Department of Internal Medicine III, University Medical Center Mainz, Mainz, Germany
[21] Institute of Epidemiology, Biometry and Statistics, Mainz, Germany
[22] Department of Medicine, Medical Clinic III, Ludwig-Maximilians-University Hospital, Munich, Germany
[23] Department of Hematology, Oncology and Rheumatology, Heidelberg University Hospital, Heidelberg, Germany

Background: Chimeric antigen receptor T-cells have revolutionized treatment in many B-cell neoplasias. In MCL, brexucabtagene autoleucel (brexu-cel) has been the first product approved based on results of the ZUMA-2 trial for patients failing prior chemoimmunotherapy and BTK-inhibitor. However, in ZUMA-2, strict criteria have been used for patient selection, e.g. no use of intensive bridging/holding treatment was allowed, excluding patients with high treatment needs. In contrast to this, in the real-world scenario patient selection is much more diverse questioning whether the results of controlled trials can be reproduced in the regular treatment landscape. In this intent, we have analyzed the results obtained with brexu-cel as standard-of-care treatment (SOC) of r/r MCL in Germany and Switzerland.

Patients/methods: Eligible for this first analysis of an ongoing registry study were all German and Swiss patients with r/r MCL who have been treated with SOC brexu-cel since 09/2020 and were registered with the German Stem Cell Registry (DRST) and the Registry of the European Mantle Cell lymphoma (EMCL), respectively. Of note, some patients have received more than one CAR-T-treatment. Data were analyzed for patient and disease characteristics, prior treatment history, response to treatment, and complications as well as post treatment outcomes. Due to the character of this analysis based on real world data, with heterogeneous surveillance strategies we have used primarily time to next treatment (TTNT) instead of progression-free survival, due to the potential biases for the latter. While still adding patients to the analysis, an additional follow-up data cut is planned 10/2023.

Results: 111 patients have been identified: median age at diagnosis was 64.3 years (range 42.3-79.5; 19/99 patients $\geq$ 70), 18% female (not known (nk) 2.7%); ethnicity 66.7% Caucasian (nk 30.6%). Disease characteristics: 80/88 had stage 3/4 (91%), histology was classical in 34/57 cases (60%) and blastoid in 19/57 (33%), respectively. MIPI score was low 14/53 (26%), intermediate 17 (32%), high 21 (40%). TP53 alteration was present in 13/58 (22%), Ki67-expression was $\leq$ 30% in 18/50 (36%). TTNT for last treatment preceding CAR-T-treatment was 7.7 months. Overall survival (OS) for the entire patient population from diagnosis was 12.8 years.

Preceding CAR-T, median number of treatments was 3 (range 1-9), all patients had prior Rituximab and Ibrutinib, 62 patients (56%) had received autologous stem cell transplantation (SCT) and 11 patients had received an allogeneic SCT. Median age at this time point was 68.1 years (range 49-82y). 50/110 patients were >70 years. Bridging treatment had been used in 88/112 (79%) preceding CAR.

Based on investigator evaluation ORR was 86%, best response to CAR-T was CR in 47/76 patients (62%) and PR in 18/76 (24%). Time to death or new treatment after CAR-T was 8 months (mo) for patients $\leq$ 70y and 12 mo for patients > 70y. There was no difference for the number of prior lines ($\leq$ 3 vs. > 3). The estimated median OS was 1.9 years. 26 patients have received at least 1 additional line of treatment after progression.

Safety: Post-CAR CRS was seen in 95/114 (83%), Grade 1/2 77/95 (81%), Grade 3/4 (18%), Grade 5 (1%); ICANS was noted in 57/111 (51%), Grade 1/2 43/57 (75%), all other Grade 3/4. The rate of ICU admissions was 25/106 (24%). However, within 28 days after CAR-T-cell treatment 9/98 (9%) patients have died. Overall, in the post CAR-T-period 20 patients died of reasons other than progression: 4 CAR-related, 11 infections, 5 other/unknown.

Discussion: In this real-world analysis, we could demonstrate, despite a more heterogeneous pre-treated patient population, a high overall and complete response rate. Median post CAR-T-cell survival was promising with 1.9 years. While CRS and ICANS risks seem to be comparable to trial data, the high non-relapse mortality (NRM) observed after SOC brexu-cel for r/r MCL is a concern and warrants refinement of anti-infectious surveillance and prophylaxis. Further work focusses on the identification of potential risk factors, e.g. using risk scores such as CAR-HAEMATOTOX, EASIX, and Severe4.

Disclosures Hess: *Novartis:* Consultancy; *Roche:* Consultancy, Honoraria; *Miltenyi:* Consultancy; *ADC Therapeutics:* Consultancy, Honoraria; *Lilly:* Consultancy, Honoraria; *Astra:* Consultancy, Honoraria; *Morphosys:* Research Funding; *Incyte:* Consultancy, Honoraria, Research Funding; *BMS:* Consultancy; *Janssen:* Consultancy, Honoraria, Research Funding; *Abbvie:* Consultancy, Honoraria, Research Funding; *Kite/Gilead:* Consultancy, Honoraria, Research Funding. **Vucinic:** *Takeda:* Consultancy, Honoraria; *MSD:* Consultancy, Honoraria; *Sobi:* Honoraria, Other: Travel/Accommodations/Expenses; *Amgen:* Honoraria; *AstraZeneca:* Honoraria; *Janssen:* Honoraria; *Gilead/Kite:* Consultancy, Honoraria; *BMS/Celgene:* Consultancy, Honoraria, Other: Travel/Accommodations/Expenses; *Novartis:* Consultancy, Honoraria; *Abbvie:* Honoraria. **Rejeski:** *Kite/Gilead:* Other: Travel Support, Research Funding; *Novartis:* Honoraria; *BMS/CELGENE:* Consultancy, Honoraria; *Pierre-Fabre:* Other: Travel Support. **Penack:** *Gilead, Jazz, MSD, Novartis, Pfizer and Therakos:* Honoraria, Other: Travel support; *Incyte and Priothera:* Research Funding; *Equillium Bio, Jazz, Gilead, Novartis, MSD, Omeros, Priothera, Sanofi, Shionogi and SOBI:* Membership on an entity's Board of Directors or advisory committees. **Koenecke:** *Pierre Fabre:* Consultancy; *Kite/Gilead:* Consultancy; *Sanofi-Aventis:* Consultancy, Speakers Bureau; *Janssen:* Consultancy, Speakers Bureau; *Miltenyi Biotec:* Consultancy; *Roche:* Consultancy, Speakers Bureau; *Pfizer:* Consultancy; *Novartis:* Consultancy, Speakers Bureau; *Medigene:* Consultancy; *Amgen:* Consultancy; *Glaxo Smith Kline:* Consultancy; *BMS:* Consultancy. **von Bonin:** *Janssen:* Research Funding; *BMS:* Other: Advisory Board; *Novartis:* Other: Advisory Board; *Kite:* Other: Advisory Board. **von Tresckow:** *Pfizer:* Consultancy; *Amgen:* Consultancy; *Roche:* Consultancy, Honoraria, Other: Travel Support; *Pentixapharm:* Consultancy; *Noscendo:* Consultancy; *Gilead Kite:* Consultancy, Other: Travel Support; *Incyte:* Consultancy, Honoraria; *Cerus:* Consultancy; *MSD:* Consultancy, Honoraria, Other: Travel Support, Research Funding; *AbbVie:* Other: Travel Support; *AstraZeneca:* Honoraria, Other: Travel Support; *Lilly:* Consultancy, Honoraria, Other: Travel Support; *Pierre Fabre:* Other: Travel support; *Miltenyi:* Consultancy; *IQVIA:* Consultancy; *BMS/Celgene:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria, Other: Travel Support, Research Funding; *Allogene:* Consultancy; *Takeda:* Consultancy, Honoraria, Other: Travel Support, Research Funding. **Stilgenbauer:** *Abbvie:* Consultancy, Honoraria, Other: travel support, Research Funding; *Sunesis:* Consultancy, Honoraria, Other: travel support, Research Funding; *Celgene:* Consultancy, Honoraria, Other: travel support, Research Funding; *Gilead:* Consultancy, Honoraria, Other: travel support, Research Funding; *GSK:* Consultancy, Honoraria, Other: travel support, Research Funding; *Roche:* Consultancy, Honoraria, Other: travel support, Research Funding; *Janssen:* Consultancy, Honoraria, Other: travel support, Research Funding; *Novartis:* Consultancy, Honoraria, Other: travel support, Research Funding; *AstraZeneca:* Consultancy, Honoraria, Other: travel support, Research Funding; *Amgen:* Consultancy, Honoraria, Other: travel support, Research Funding. **Schroers:** *BMS:* Consultancy, Honoraria; *Janssen:* Consultancy, Honoraria; *GSK:* Consultancy, Honoraria. **Duell:** *MorphoSys AG, Regeneron:* Research Funding. **Mueller:** *AstraZeneca, BMS, Gilead, Janssen, Miltenyi biomedicine, Novartis:* Consultancy; *Mil-*

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