New stratification and treatment approaches in ALL - including CAR T Cell therapy

Sabina Chiaretti, Renato Bassan, Antonella Vitale, Loredana Elia, et al.

A DASATINIB-BLINATUMOMAB COMBINATION FOR THE FRONT-LINE TREATMENT OF ADULT PH+ ALL PATIENTS. PRELIMINARY RESULTS OF THE GIMEMA LAL2116 D-ALBA TRIAL; ON BEHALF OF GIMEMA ACUTE LEUKEMIA WORKING PARTY

Conclusion: This is the first chemo-free induction-consolidation protocol for adult Ph+ ALL patients of all ages based on a combination of a targeted and immunotherapeutic strategy. Though preliminary, the rates of molecular responses and survival are highly promising.

Stephan Grupp, Shannon Maude, Andre Baruchel, Theodore W. Laetsch, et al.

TISAGENLECLEUCEL APPEARS EFFECTIVE AND SAFE IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH RELAPSED/REFRACTORY ACUTE LYMPHOBLASTIC LEUKEMIA WITH HIGH-RISK CYTOGENETIC ABNORMALITIES

Conclusion: In pts with HR cytogenetic abnormalities with historically poor prognosis, tisagenlecleucel appears effective, with high rates of durable responses, prolonged survival, and a manageable safety profile.

Nicola Goekbuget, Hervé Dombret, Gerhard Zugmaier, Massimiliano Bonifacio, et al.

BLINATUMOMAB FOR MINIMAL RESIDUAL DISEASE (MRD) IN ADULTS WITH BCELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA (BCPALL): MEDIAN OVERALL SURVIVAL (OS) NOT REACHED AT 5 YEARS FOR COMPLETE MRD RESPONDERS

Conclusion: In the final, 5-year follow-up analysis of a multinational study of adults with BCP-ALL in hematologic complete remission with MRD, median OS was 36.5 months after blinatumomab treatment. Median OS was not reached among patients with a complete MRD response in cycle 1 of blinatumomab treatment. These results provide further support for long-term OS benefits associated with blinatumomab

treatment in adults with BCP-ALL and MRD.

Anna Candoni, Davide Lazzarotto, Antonio Curti, Felicetto Ferrara, et al.

NELARABINE AS SALVAGE THERAPY AND BRIDGE TO ALLOGENEIC STEM CELLS TRANSPLANTATION IN 118 ADULT PATIENTS WITH RELAPSED/REFRACTORY T-ACUTE LYMPHOBLASTIC LEUKEMIA/LYMPHOMA. A CAMPUS-ALL, PHASE 4, STUDY.

Conclusion: This is one of the largest cohort of adult patients with relapsed or refractory T-ALL/T-LBL treated in real-world with Nelarabine. Taking into account the poor prognosis of this population Nelarabine can be considered as an effective option providing an ORR of 50% and a CR rate of 36%. In addition, 40% of cases who received Nelarabine salvage therapy underwent an Allo-SCT with an expected OS at 2 and 5 years of 46% and 38%, respectively. Overall, the safety profile of Nelarabine was acceptable with only 8 % of cases with grade III-IV neurological AE.

Anthony Moorman, Amy Kirkwood, Amir Enshaei, Laura Clifton-Hadley, et al.

CLINICAL EFFICACY OF A NOVEL VALIDATED PROGNOSTIC INDEX FOR TRIAL DESIGN IN ADULT ACUTE LYMPHOBLASTIC LEUKAEMIA.

Conclusion: PIUKALL, which was developed and validated using paediatric ALL data, is a valid and powerful biomarker in adult ALL. This intriguing observation highlights the benefit of integrating risk factors as continuous variables. We have demonstrated how PIUKALL could be used to provide additional prognostic information in treatment scenarios previously allocated by binary decision. We plan to use this risk score when designing our next adult ALL trial, UKALL15.

Choice of Poster Presentations

Dragana Slavkovic Lukic, Johannes Duell, Jan Davidson-Moncada, Andreas Schlagowsky, et al.

COMBINATION OF FLOTETUZUMAB, A CD123 X CD3 BISPECIFIC DART® MOLECULE, AND BLINATUMOMAB, A CD19 X CD3 BITE MOLECULE, TO PREVENT ANTIGEN ESCAPE IN B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIAB-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA

Conclusion: Our results indicate that dual targeting of CD123 and CD19 with combination of low doses

of flotetuzumab and blinatumomab is an attractive approach to prevent antigen escape of BCP-ALL, resulting in significant reduction of cytokine production by effector cells.

Veerle Mondelaers, Tim Lammens, Laurence Dedeken, Anne Uyttebroeck, et al.

NATION-WIDE PROSPECTIVE, REAL-TIME MONITORING OF PEGYLATED E.COLI AND ERWINIA ASPARAGINASE THERAPY IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA AND NON-HODGKIN LYMPHOMA IN BELGIUM

Conclusion: This prospective nation-wide, multi-center study shows that monitoring of ASNase activity during treatment of children with ALL and NHL is feasible and informative. Allergy and SI occurred after both peg-ASNase and Erwinia ASNase administration.

Soumika Sengupta, Mainak Biswas, Khushboo Gandhi, Vikram Gota, Avinash Sonawane

IN VITRO AND IN VIVO STUDIES OF NOVEL ASPARAGINASE MUTANTS FOR THE TREATMENT OF ACUTE LYMPHATIC LEUKEMIA

Conclusion: Considering all parameters, Mutant B was found to have the most favorable characteristics and emerged as the lead candidate for future development. This formulation is expected to overcome the existing deficiencies and clinical challenges encountered with the EcA formulations. Clinical development of this drug candidate is envisaged.

Paroni Fan, Kathy Chan, Terry Chow, Grace Lam, Frankie Cheng, Chi-kong Li

ASPARAGINASE ACTIVITY AND ANTI- E. COLI ASPARAGINASE ANTIBODY LEVEL MONITORING FOR DIFFERENT ASPARAGINASE PREPARATIONS IN HONG KONG CHILDHOOD ALL PATIENTS

Conclusion: Our results high incidence of allergy to Leunase in Chinese children. Patients allergic to Leunase were either clinically hypersensitive or silently inactivated to Oncaspar, suggesting that Oncaspar may not be a suitable alternative after Leunase allergy while the two brands of Erwinia asparaginase displayed satisfactory efficacy without triggering much hypersensitive response. Given the specificity and sensitivity, measurement of asparaginase activity should be part of the clinical monitoring to ensure adequate efficacy of different preparations.

Matthias Stelljes, *Elias* Jabbour, *Anjali* Advani, *Daniel J* DeAngelo, et al.

INOTUZUMAB OZOGAMICIN (INO) TREATMENT IN PATIENTS WITH RELAPSED/REFRACTORY ACUTE LYMPHOBLASTIC LEUKEMIA (R/R ALL): OUTCOMES OF PATIENTS TREATED IN SALVAGE ONE WITH A LONG DURATION OF FIRST REMISSION

Conclusion: Improved outcomes were seen with InO vs SC among S1 pts who had a long first complete remission (CR1 ≥ 12 mos or CR1 ≥ 18 mos), supporting the benefit of InO vs SC in this population.

David I Marks, Daniel J DeAngelo, Elias Jabbour, Anjali Advani, et al.

MORE OR LESS? IMPACT OF DOSE NUMBER ON OUTCOMES OF PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED WITH INOTUZUMAB OZOGAMICIN

Conclusion: These results are in agreement with current recommendations that patients proceeding to SCT should receive ≤2 Cyc, whereas those not proceeding to SCT may benefit from receiving up to 6 cycles of therapy.

Elias Jabbour, Matthias Stelljes, Anjali Advani, Daniel J DeAngelo, et al.

TIME FROM RANDOMIZATION TO FIRST SUBSEQUENT INDUCTION/SALVAGE THERAPY IN PATIENTS WITH RELAPSED/REFRACTORY ACUTE LYMPHOBLASTIC LEUKEMIA TREATED WITH INOTUZUMAB OZOGAMICIN IN THE PHASE 3 INO-VATE TRIAL

Conclusion: In this study, treatment with InO provided the benefit of extended TST, effectively allowing patients a longer time period until an ST was needed in both patients who proceeded to as well as those who did not proceed to HSCT.

Marie Emilie Dourthe, Aurélie Cabannes-Hamy, Karima Yakouben, Florence Fabian, et al.

SAFETY AND EFFICACY OF TISAGENLECLEUCEL (CTL019) IN B ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN AND YOUNG ADULTS: ROBERT DEBRÉ AND SAINT LOUIS HOSPITALS EXPERIENCE

Conclusion: CTL019 confirms its efficacy in a cohort of patients heavily pretreated for refractory or relapsed B-ALL without additional therapy after remission. The toxicity profile underlines the need of a strong collaboration between intensivists, neurologists and hematologists to successfully manage these patients.

Bijal D. Shah, Michael R. Bishop, Olalekan O. Oluwole, Aaron C. Logan, et al.

KTE-X19, AN ANTI-CD19 CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY, IN ADULT PATIENTS WITH RELAPSED/REFRACTORY ACUTE LYMPHOBLASTIC LEUKEMIA: END OF PHASE 1 RESULTS OF ZUMA-3

Conclusion: KTE-X19 dosing and safety management have been successfully refined by testing 3 cell doses and evaluating a new AE management guideline with altered corticosteroids/tocilizumab use for NEs/CRS. The pivotal Phase 2 portion of ZUMA-3 is ongoing at the 1 × 106 dose with revised AE management.

Jia Chen, Xiang Zhang, Yi Fan, Aining Sun, et al.

CAR-T CELL THERAPY BRIDGING TO ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION LED TO SUPERIOR SURVIVAL FOR ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS OUT OF REMISSION

Conclusion: Our data showed, for B-cell ALL patients out of remission, CAR-T cell therapy targeting to CD19/CD22 had a promising response but long-term outcome remained poor. Sequential allogeneic HCT may dramatically improve the OS and PFS, which needs to be further validated by randomized studies.

Heng Mei, Yu Hu, Huiwen Jiang, Fen Zhou, et al.

ANTI-CD19 CAR-T THERAPY BRIDGING TO ALLO-HSCT IMPROVES LONG-TERM OUTCOME OF B-ALL PATIENTS WITH HIGH LEUKEMIA BURDEN OR POOR PROGNOSTIC MARKERS

Conclusion: These data demonstrate that CAR-T therapy bridging to allo-HSCT is a safe and effective therapeutic strategy for r/r B-ALL patients, and can achieve better efficacy in terms of maintaining long-term EFS and RFS. Patients with high pre-infusion MRD or with poor prognostic markers can benefit from the early consolidative allo-HSCT after CAR-T therapy. Trials were registered at www.clinicaltrials.gov as # NCT02965092 and # NCT03366350.

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Huiwen Jiang, Heng Mei, Yu Hu, Tao Guo, et al.

IMPROVING THE SAFETY OF CAR-T CELL THERAPY BY CONTROLLING CRS-RELATED COAGULOPATHY

Conclusion: To conclude, coagulation disorders frequently happen during CAR-T therapy. TF and PECAM-1 are of great importance in the etiology and pathogenesis of coagulation problems. Early and proper interventions targeted at CRS-related coagulopathy contribute a lot to the control of side effects in CAR-T therapy. This trial was registered at www.clinicaltrials.gov as # NCT02965092.