(S102) FIRST RESULTS OF THE APOLLO TRIAL: A RANDOMIZED PHASE III STUDY TO COMPARE ATO COMBINED WITH ATRA VERSUS STANDARD AIDA REGIMEN FOR PATIENTS WITH NEWLY DIAGNOSED, HIGH-RISK ACUTE PROMYELOCYTIC LEUKEMIA

Topic: 4. Acute myeloid leukemia - Clinical

Uwe Platzbecker¹, Lionel Adès², Pau Montesinos³, Emanuele Ammatuna⁴, Pierre Fenaux⁵, Claudia Baldus⁶, Céline Berthor⁶, Monica Bocchia⁷, Caroline Bonmati⁸, Erika Borleihg⁹, Martin Bornhauser¹⁰, Diana Carp¹¹, Sylvain Chantepie¹², Fatihah Cherrat¹³, Fabio Ciciri¹⁴, Enrico Crea¹⁵, Hartmut Döhner¹⁶, Gerhard Ehninger¹⁰, Jordi Esteve Reyner¹⁷, Jamilé Frayfer¹⁸, Gianluca Gaidano¹⁹, Ana Garrido Díaz₂⁰, Cristina Gi³²¹, Livia Gorreo Renzulli¹⁵, Anna Franziska Hamm²², Mael Heiblig²³, Daniela Heidenreich²⁴, Madlen Jentschsch¹, Alwin Johannes Krämer²⁵, Marie-Pierre Ledoux²⁶, Valentina Mancini²⁷, Klaus Metzelo²⁸, Maria Cristina Miggiano²⁹, Carsten Müller-Tidow²⁵, Dietger Niedewiase²⁸, Pierre Peterlin³⁰, Kathrin Riegler¹⁰, Christoph Röllig¹⁰, Giovanni Rossi³², Miguel A Sanz²¹, Hubert Serve³³, Maaike Sohne³⁴, Karsten Spiekermann³⁵, Emmanuelle Tavernier-Tardy³⁶, Christian Thiede¹⁰, Susana Vives Polo³⁷, Wichard Vogel³⁸, Michaela Weiβer¹⁰, Patrizia Zappasodi³⁹, Pauline Ziller-Walther¹⁰, Sven Zukunft¹⁰, Francesco Lo Coco⁴⁰, Maria Teresa Voso⁴⁰

¹University Hospital Leipzig, Department for Hematology, Cellular Therapy and Hemostaseology, Leipzig, Germany; ²Hôpital Saint Louis, Service d'Hématologie Sénior, Paris, France; ³Hospital Universitari i Politécnic La Fe, Servicio de Hematología, Valencia, Spain; ⁴University Medical Center Groningen, Afd. Hematologie, Groningen, The Netherlands; ⁵University Hospital Schleswig-Holstein, Department of Internal Medicine II, Kiel, Germany; ⁶Le Centre Hospitalier Universitaire de Lille, Service des Maladies du sang, Lille, France; ⁷Azienda Ospedaliero-Universitaria di Siena, Ematologia, Siena, Italy; ⁸Le Centre Hospitalier Régional Universitaire de Nancy, Service d'Hématologie et Médecine Interne, Vandoeuvre-lès-Nancy, France; ⁹ASST degli Spedali Civili di Brescia, Ematologia, Brescia, Italy; ¹⁰TUD Dresden University of Technology - Faculty of Medicine Carl Gustav Carus, Medical Clinic I, Dresden, Germany; ¹¹Le Centre Hospitalier Régional d'Orléans, Service d'Hématologie Clinique et de Thérapie Cellulaire, Orléans, France; ¹²Le Centre Hospitalier Universitaire de Caen, Service d'Hématologie Clinique, Caen, France; ¹³Groupe Francophone des Myélodysplasies (GFM), Hospital Saint Louis, Service d'Hématologie Sénior, Paris, France; ¹⁴Ospedale San Raffaele S.r.l. U.O. Ematologia e Trapianto di Midollo, Milano, Italy; ¹⁵Fondazione GIMEMA Franco Mandelli Onlus, Roma, Italy; ¹⁶Universitätsklinikum Ulm, Department of Internal Medicine III, Ulm, Germany; ¹⁷Hospital Universitario de Canarias, Servicio de Hematología, Santa Cruz de Tenerife, Spain; ¹⁸Centre Hospitalier de Meaux, Service d'Hématologie, Meaux, France; ¹⁹Azienda Ospedaliero-Universitaria Maggiore della Carità di Novara, Ematologia, Novara, Italy; ²⁰Hospital de la Santa Creu i Sant Pau, Servicio de Hematologia, Barcelona, Spain; ²¹Hospital General Universitario de Alicante, Servicio de Hematologia, Alicante, Spain; ²²University Hospital Schleswig-Holstein, Medical Clinic I, Lübeck, Germany; ²³Hospices Civils de Lyon - Lyon-Sud Hospital, Department of Hematology, Pierre Bénite, France; ²⁴University Hospital Mannheim, Medical Clinic III, Mannheim, Germany; ²⁵University Hospital Heidelberg, Department of Internal Medicine 5, Heidelberg, Germany; ²⁶Institut de cancérologie Strasbourg Europe, Strasbourg, France; ²⁷ASST Grande Ospedale Metropolitano Niguarda, Ematologia, Milano, Italy; ²⁸University Hospital Leipzig, Department for Hematology and Cellular Therapy, Leipzig, Germany; ²⁹Azienda ULSS 8 Bercia, Ematologia, Vicenza, Italy; ³⁰Le Centre Hospitalier Universitaire de Nantes, Service d'Hématologie Clinique, Nantes, France; ³¹Charité - University Medicine Berlin - Campus Benjamin Franklin, Medical Clinic III, Berlin, Germany; ³²Ospedale Casa Sollievo della Sofferenza, Ematologia, San Giovanni Rotondo, Italy; ³³Goethe University Frankfurt, Dept. of Medicine II, Frankfurt a. M., Germany; ³⁴St. Antonius Ziekenhuis, Nieuwegein, The Netherlands; ³⁵University Hospital Grosshadern - Ludwig-Maximilians-University, Department of Medicine III, München, Germany; ³⁶Institut De Cancérologie Et D'Hématologie Universitaire De Saint-Etienne, Saint-Priest-en-Jarez, France; ³⁷Hospital Universitari Germans Trias i Pujol, Servicio de Hematologia, Barcelona, Spain; ³⁸University Hospital Tübingen, Department of Hematology, Oncology, Clinical Immunology and Rheumatology, Tübingen, Germany; ³⁹Fondazione IRCCS Policlinico San Matteo, S.C. Ematologia, Pavia, Italy; ⁴⁰Fondazione PTV Policlinico Tor Vergata, U.O.S.D. Diagnostica Avanzata Oncoematologica, Rome, Italy;

Background:

Pioneered by the APL0406 trial (Lo-Coco et al., NEJM 2013), prior investigations have demonstrated the superiority of combining all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) over standard ATRA and chemotherapy (CHT) as

Copyright Information: (Online) ISSN: 2572-9241
© 2024 The Author(s), HemaSphere published by John Wiley & Sons Ltd on behalf of European Hematology Association. This is an open access Abstract Book distributed under the Attribution-NonCommercial-NoDerivs (CC BY-NC-ND), which allows third parties to download the articles and share them with others as long as they credit the author and the Abstract Book, but they cannot change the content in any way or use them commercially.

Abstract Book Citations: Authors, Title, HemaSphere, 2024;8(S1):pages.
front-line management of low/intermediate risk acute promyelocytic leukemia (APL). However, the efficacy of ATRA/ATO in high-risk APL (HR-APL), defined as >109/L white blood cell counts (WBC) at diagnosis, has not been studied within randomized trials so far.

Aims:

The objective of the APOLLO trial was to prospectively compare the efficacy of the ATRA-ATO regimen (arm A) versus the standard of care (ATRA-CHT; arm B) in patients with HR-APL.

Methods:

The APOLLO trial (NCT0268840) is an open-label, randomized European intergroup trial. Eligible pts are aged 18-65 years with newly diagnosed HR-APL. Patients in the ATRA-ATO arm received two doses of idarubicin (12 mg/m2) on day 1 and 3, plus ATO 0.15 mg/kg and ATRA 45 mg/m2, daily until CR. Consolidation consisted of 4 courses of ATO 5 days/week, 4 weeks on 4 weeks off, for a total of 4 courses, in parallel with ATRA 2 weeks on and 2 weeks off (7 courses). Patients in the ATRA-CHT arm received the standard AIDA (ATRA+Idarubicin) induction followed by 3 cycles of CHT-based consolidation as well as maintenance. The primary study endpoint is EFS at 2 years including the following events: no achievement of CR after induction therapy; no achievement of molecular remission after consolidation; relapse (hematological/molecular); death including early death or development of secondary myelodysplasia or leukemia. Secondary endpoints include overall survival (OS), toxicity, measurable residual disease and quality of life assessments. ATO was provided free of charge by TEVA pharmaceuticals. The project was funded by the German Federal Ministry of Education and Research.

Results:

The study was prematurely discontinued in August 2022, due to slow recruitment during the Covid-19 pandemic, and expiration of study-drug reserved for the trial. Maintenance treatment and observational period are still ongoing. Overall, 131 patients are evaluable for outcome, 68 in Arm A and 63 in arm B. Median WBC was 36 x109/L (10.1-489.0 x109/L) and 39% had WBC > 50 x109/L. CR+CRi was achieved in 63/68 (93%) in the ATRA-ATO versus 57/63 (91 %) in the ATRA-CHT arm (P= 0.65). Early death rate was similar across arms (5 and 7 pts in the ATRA-ATO and ATRA-CHT arm, respectively). Causes of early death were bleeding in 3 and 4, sepsis in 0 and 2, thrombosis in 1 and 1, pulmonary failure due to leucostasis related to APL in 1 and 0 pts in the ATRA-ATO and ATRA-CHT arm, respectively. A total of 120 out of 131 patients are currently evaluable for disease status following induction. After a median follow-up of 31 months (range 1.7 – 71.5 months), the 2-year EFS was 89% and 72% in the ATRA-ATO and ATRA-CHT groups respectively (P= 0.02, Figure 1). Molecular relapse was observed in 0 and 6 pts in the ATRA-ATO and ATRA-CHT arm, respectively. The 2-year OS rate was 93% vs 87% (P= 0.33) for ATRA-ATO vs ATRA-CHT, respectively. Death in CR/CRi were observed in 0 and 3 pts in the ATRA-ATO and ATRA-CHT arm, respectively. Analysis of safety is ongoing.

Summary/Conclusion:

First-line therapy with ATRA-ATO with two initial doses idarubicin results in superior EFS compared to conventional ATRA-CHT in patients with HR-APL. Further analysis of the APOLLO trial may support the implementation of this regimen as the new standard of care in patients with HR-APL.