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Conference Coverage: ASH 2022 – Focus on Leukemia

Wednesday, December 14, 2022

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Meeting Snapshot

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VIRTUAL CLOSED-DOOR ROUNDTABLE

DATE:
December 14, 2022

DISEASE STATE AND DATA PRESENTATIONS by key experts

INSIGHTS REPORT including postmeeting analyses and actionable recommendations

PANEL: Key experts in leukemia

- 6 from US
- 3 from Europe

LEUKEMIA-SPECIFIC DISCUSSIONS on latest research updates, therapeutic advances, and their application in clinical decision-making

Panel Consisting of 6 US and 3 European Leukemia Experts

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CHAIR:
Elias Jabbour, MD
MD Anderson Cancer Center

Jae Park, MD
Memorial Sloan Kettering Cancer Center

Gail J. Roboz, MD
Weill Cornell Medicine

Amir Fathi, MD
Massachusetts General Hospital Cancer Center

Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil
Queen Elizabeth Hospital

Uwe Platzbecker, MD
University Hospital Leipzig

Naval Daver, MD
MD Anderson Cancer Center

Rami Komrokji, MD
Moffitt Cancer Center

Josep-Maria Ribera, MD, PhD
Catalan Institute of Oncology

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Meeting Agenda (1/2)

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Time	Topic	Presenter
11.00 AM – 11.05 AM (5 min)	Welcome and Introduction	Elias Jabbour, MD
New Developments in Myelodysplastic Syndromes (MDS)		
11.05 AM – 11.10 AM (5 min)	**Low-Risk Disease**	Rami Komrokji, MD
11.10 AM – 11.15 AM (5 min)	• **High-Risk Disease** • **Others**	Uwe Platzbecker, MD
11.15 AM – 11.35 AM (20 min)	Discussion	All
11.35 AM – 11.40 AM (5 min)	Key Takeaways	Rami Komrokji, MD, and Uwe Platzbecker, MD
Advances in Acute Myeloid Leukemia (AML): Newly Diagnosed		
11.40 AM – 11.45 AM (5 min)	**Commercially Available Therapies, Excluding Transplantation and Cellular Immunotherapies**	Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil
11.45 AM – 11.55 AM (10 min)	• **Investigational Therapies, Excluding Transplantation and Cellular Immunotherapies** • **Advances in Mutation-Targeted Therapy**	Naval Daver, MD
11.55 AM – 12.20 PM (25 min)	Discussion	All
12.20 PM – 12.25 PM (5 min)	Key Takeaways	Charles Craddock, CBE, FRCP (UK), FRCPath, DPhil, and Naval Daver, MD

Meeting Agenda (2/2)

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Time	Topic	Presenter
Advances in AML: Relapsed/Refractory		
12.25 PM – 12.35 PM (10 min)	• **Commercially Available Therapies, Excluding Transplantation and Cellular Immunotherapies** • **Investigational Therapies, Excluding Transplantation and Cellular Immunotherapies** • **Biomarkers, Molecular Markers, and MRD**	Gail J. Roboz, MD
12.35 PM – 12.50 PM (15 min)	Discussion	All
12.50 PM – 12.55 PM (5 min)	Key Takeaways	Gail J. Roboz, MD
12.55 PM – 1.05 PM (10 min)	*BREAK*	
Advances in Acute Lymphoblastic Leukemia (ALL): Newly Diagnosed		
1.05 PM – 1.15 PM (10 min)	**ALL Therapies, Excluding Transplantation and Cellular Immunotherapies: Clinical Trials**	Josep-Maria Ribera, MD, PhD
1.15 PM – 1.20 PM (5 min)	**Management of Novel ALL Subsets in Different Age Groups**	Amir Fathi, MD
1.20 PM – 1.40 PM (20 min)	Discussion	All
1.40 PM – 1.45 PM (5 min)	Key Takeaways	Josep-Maria Ribera, MD, PhD, and Amir Fathi, MD
Advances in ALL: Relapsed/Refractory		
1.45 PM – 1.50 PM (5 min)	**ALL Therapies, Excluding Transplantation and Cellular Immunotherapies: Clinical Trials**	Jae Park, MD
1.50 PM – 2.05 PM (15 min)	Discussion	All
2.05 PM – 2.10 PM (5 min)	Key Takeaways	Jae Park, MD
2.10 PM – 2.15 PM (5 min)	Summary and Closing Remarks	Elias Jabbour, MD

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New Developments in MDS

Conference Highlights From ASH 2022

Phase II/III IMerge: Imetelstat in pts with heavily transfused non-del(5q) LR-MDS R/R to erythropoiesis-stimulating agents

Uwe Platzbecker, et al. 2022, ASH #459

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STUDY POPULATION

> Pts with LR MDS (IPSS low or intermediate-1), R/R to ESA or sEPO >500 mU/mL, and TD

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Phase III Sintra-REV: Final results of low-dose LEN (5 mg) vs placebo in non–transfusion-dependent LR del(5q) MDS

Félix López Cadenas, et al. 2022, ASH #460

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STIMULUS-MDS1 and MDS2: Disease characteristics and international scoring systems in adult pts with HR-MDS participating in 2 randomized, double-blind, placebo-controlled studies with IV sabatolimab added to HMA

Valeria Santini, et al. 2022, ASH #559

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STUDY POPULATION

> Pts ≥18 years old with IR/HR/vHR-MDS per IPSS-R not eligible for SCT or intensive chemotherapy

Phase II STIMULUS-MDS1: Primary results of sabatolimab added to HMAs in adult pts with HR-MDS

Amer M. Zeidan, et al. 2022, ASH #853

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STUDY POPULATION

- Treatment-naive pts aged ≥18 years with IR/HR/vHR-MDS defined by IPSS-R

Phase III ASCERTAIN: Oral decitabine/cedazuridine in biallelic *TP53*mut MDS

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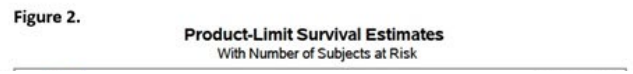
Michael R. Savona, et al. 2022, ASH #854

STUDY POPULATION

- 133 pts with MDS/CMML



Phase II: Canakinumab in LR-MDS

Guillermo Garcia-Manero, et al. 2022, ASH #858

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STUDY POPULATION

- Pts aged ≥18 years with IPSS-R ≤3.5 MDS, normal renal and hepatic function, and PS who had previously received >1 line of therapy

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New Developments in MDS

Key Insights

Key Takeaways: New Developments in MDS (1/3)

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LR-MDS

#459: Imetelstat achieved prolonged, continuous transfusion independence in pts with heavily transfused

According to a recent press release, the COMMANDS trial met its primary endpoint, showing a highly statistically significant and clinically meaningful improvement in RBC-TI with concurrent Hb increase in the 1L treatment of adult patients with very low-, low-, or intermediate-risk MDS who require RBC transfusions. https://news.bms.com/news/details/2022/Bristol-Myers-Squibb-Announces-Positive-Topline-Results-of-Phase-3-COMMANDS-Trial/default.aspx

Key Takeaways: New Developments in MDS (2/3)

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LR-MDS

#858: Clinical and biological effects of canakinumab in LR-MDS: results from a phase II clinical trial (Guillermo Garcia-Manero, et al)

Key Takeaways: New Developments in MDS (3/3)

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HR-MDS

#559: Disease characteristics and international prognostic scoring systems (IPSS, IPSS-R, IPSS-M) in adult pts with HR-

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Advances in Newly Diagnosed AML

Conference Highlights From ASH 2022

Phase I/II: AZA + VEN and magrolimab in pts with newly diagnosed older/unfit or HR AML and R/R AML

Naval Daver, et al. 2022, ASH #61

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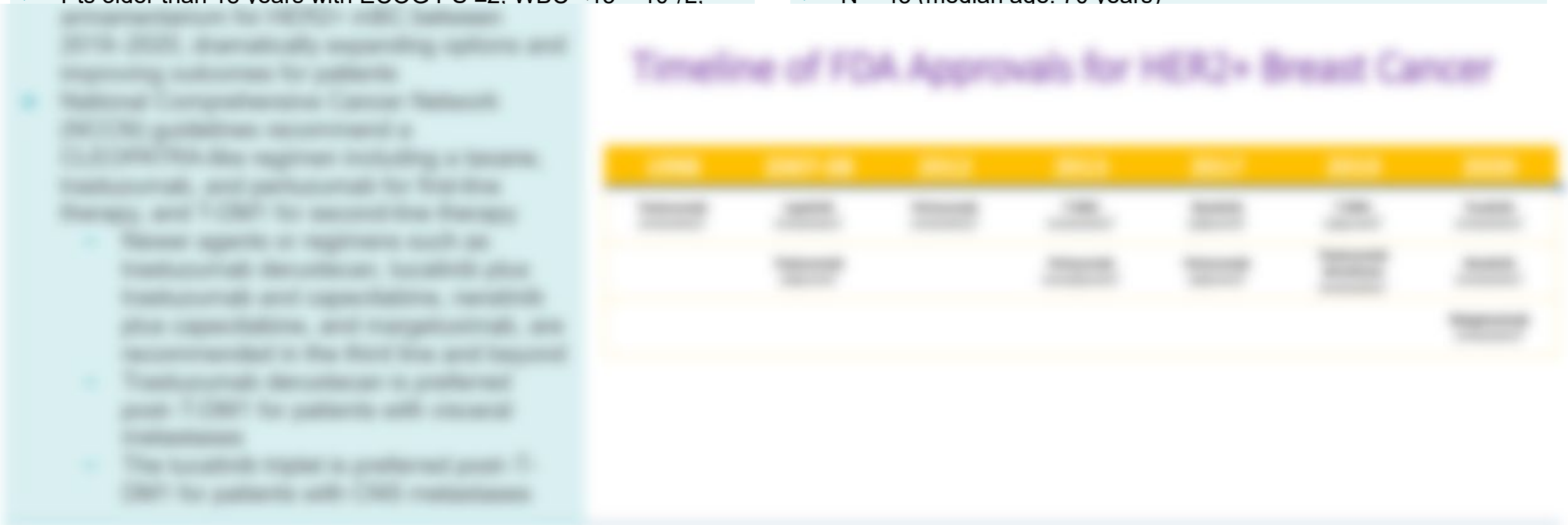
STUDY POPULATION AND DESIGN

- Pts older than 18 years with ECOG PS ≤2, WBC <15 × 10^9/L,

OUTCOME (FRONTLINE PATIENTS)

- N = 43 (median age: 70 years)



Phase III UK NCRI AML 19: FLAG-Ida + GO in younger pts with newly diagnosed AML

Nigel H. Russell, et al. 2022, ASH #218

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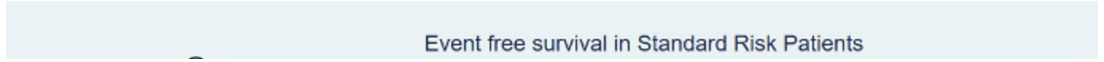
STUDY POPULATION

- Newly diagnosed AML/MDS-EB2 not known to have adverse



Phase III VIALE-A: Long-term FU of VEN-AZA for pts with untreated AML ineligible for intensive chemotherapy

Keith W. Pratz, et al. 2022, ASH #219

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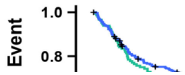
STUDY POPULATION

- Pts with confirmed AML who were previously untreated and ineligible for

Figure 1. Overall Survival



Real-world: “7+3” intensive chemotherapy vs VEN-HMA for initial therapy in adult AML

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Andrew Matthews, et al. 2022, ASH #426

STUDY RATIONALE AND POPULATION

> Exploration of comparative effectiveness of VEN-HMA as an induction regimen vs “7+3” in fit adults with newly diagnosed AML

Phase II: VEN + CLIA as induction therapy for newly diagnosed AML and HR-MDS

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Patrick K. Reville, et al. 2022, ASH #709

STUDY POPULATION

> Pts with previously untreated AML or HR-MDS (≥10% blasts or IPSS ≥2),

DOSING

Phase I/II Gimema AML1718: Interim analysis of VEN, fludarabine, idarubicin, and cytarabine as induction therapy of non-LR AML

Giovanni Marconi, et al. 2022, ASH #710

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METHODS AND STUDY DESIGN

> Modified 2-stage Simon's design: 2 consecutive 6-pt safety run-in

OUTCOME

> N = 57 (median age: 54 years)

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Phase I CAVEAT: Updated analysis of venetoclax in elderly AML

Chong Chyn Chua, et al. 2022, ASH #711

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STUDY POPULATION AND DESIGN

> Pts aged ≥65 years with de novo or

OUTCOME

> N = 69 (median age: 72 years)

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Phase I/II: Updated results of the triplet combination of VEN-AZA and gilteritinib for pts with *FLT3*mut AML

Nicolas Short, et al. 2022, ASH #831

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STUDY POPULATION AND DESIGN

> Pts with either R/R *FLT3*mut AML or de novo

OUTCOME

> N = 47 (de novo, n = 27; R/R, n = 20)

Phase III AMLSG 09-09: GO + intensive chemotherapy for pts with *NPM1*mut AML

Hartmut Döhner, et al. 2022, ASH #832

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STUDY POPULATION

> Pts with *NPM1*mut AML (standard arm: n = 296; GO arm: n = 292)

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Advances in Newly Diagnosed AML

Key Insights

Key Takeaways: Advances in Newly Diagnosed AML (1/4)

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Commercially available therapies, excluding transplantation and cellular immunotherapies

#218: FLAG-Ida combined with GO improves EFS in younger pts with newly diagnosed AML and shows an OS benefit in *NPM1* and

Key Takeaways: Advances in Newly Diagnosed AML (2/4)

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Commercially available therapies, excluding transplantation and cellular immunotherapies (cont.)

#426: Real world effectiveness of "7+3" intensive chemotherapy vs venetoclax and HMA for initial therapy in adult AML (Andrew

[redacted]

Key Takeaways: Advances in Newly Diagnosed AML (3/4)

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Investigational therapies, excluding transplantation and cellular immunotherapies (cont.)

#710: Gimema AML1718 Part 1: Planned interim analysis of a safety run-in and phase II open-label study of venetoclax, fludarabine,

[redacted]

Key Takeaways: Advances in Newly Diagnosed AML (4/4)

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Advances in mutation-targeted therapy

#831: Updated results from a phase I/II study of the triplet combination of azacitidine, venetoclax, and gilteritinib for pts with *FLT3*mut

[redacted]

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Advances in R/R AML

Conference Highlights From ASH 2022

Phase I/II: Pivekimab sunirine + VEN-AZ in HR pts with R/R AML

Naval Daver, et al. 2022, ASH #62

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STUDY POPULATION AND DESIGN

> Pts with CD123-positive R/R AML

SAFETY

> As of June 20, 2022, preliminary safety data are available for 71

Phase I AUGMENT-101: Revumenib in *KMT2A*-rearranged or *NPM1*mut AML

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Ghayas C. Issa, et al. 2022, ASH #63

STUDY POPULATION AND DESIGN

- Adult and pediatric pts with R/R *KMT2A*-rearranged or *NPM1*mut acute leukemia

Treatment

[redacted]

remissions in pts with leukemia refractory to multiple prior lines of therapy

Phase I: Lintuzumab-Ac225 + intensive chemotherapy in R/R AML with adverse features

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Sameem Abedin, et al. 2022, ASH #65

STUDY POPULATION AND DESIGN

- Pts ≥18 years with R/R AML

CLAG-M Regimen

Lintuzumab-Ac225

Efficacy

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Phase II: VEN + FLAG-Ida in R/R AML

Sai Prasad Desikan, et al. 2022, ASH #221

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STUDY POPULATION AND DESIGN

> Pts >18 years of age with R/R AML, defined as lack of response after at

Induction

Retrospective analysis: Clinical outcomes and impact of therapeutic intervention of pts with AML with recurrence of MRD after achievement of MRD-negative remission

Walid Macaron, et al. 2022, ASH #224

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STUDY POPULATION

> Retrospective analysis of adults with AML in first morphologic remission who achieved MRD negativity by flow cytometry and subsequently had MRD-positive relapse (N = 55)

[redacted]

[redacted]

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Advances in R/R AML

Key Insights

Key Takeaways: Advances in R/R AML (1/3)

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Commercially available therapies, excluding transplantation and cellular immunotherapies

#221: Updated phase IIb results of venetoclax with FLAG-Ida in R/R AML (Sai Prasad Desikan, et al)

Key Takeaways: Advances in R/R AML (2/3)

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Investigational therapies, excluding transplantation and cellular immunotherapies (cont.)

#63: The Menin inhibitor SNDX-5613 (revumenib) leads to durable responses in pts with *KMT2A*-rearranged or *NPM1*mut AML:

Key Takeaways: Advances in R/R AML (2/2)

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Biomarkers, molecular markers, and MRD

#224: Clinical outcomes and impact of therapeutic intervention in pts with AML with recurrence of MRD after achievement of MRD-

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Advances in Newly Diagnosed ALL

Conference Highlights From ASH 2022

Phase III ECOG-ACRIN E1910: Consolidation therapy with blinatumomab in newly diagnosed pts with B-lineage ALL in MRD-negative remission

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Mark R. Litzow, et al. 2022, ASH #LBA-1

STUDY POPULATION AND DESIGN

> Pts (age 30–70) with newly diagnosed

OUTCOME

> 772 pts were screened, of whom

Figure 2: Overall Survival

Phase III AIEOP-BFM ALL 2009: Impact of additional intensive L-asparaginase during consolidation phase for HR ALL

Valentino Conter, et al. 2022, ASH #49

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STUDY POPULATION

> Between 2010–2017, 6136 pts aged 1–17 with Ph-negative ALL were enrolled

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Phase II JPLSG T-11/JALSG T-ALL-211-U: Risk stratified therapy with nelarabine and intensified administration of L-asparaginase for newly diagnosed T-cell ALL in adolescents and young adults

Yoshihiro Hatta, et al. 2022, ASH #54

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STUDY POPULATION AND DESIGN

> Reported pts were aged between 15–24 years and had newly diagnosed T-ALL (N = 62). They were stratified into 3 groups

Phase II GRAALL-2014/B QUEST: Cohort analysis of blinatumomab during consolidation in adults with HR Ph-negative BCP ALL

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Nicolas Boissel, et al. 2022, ASH #211

STUDY POPULATION AND DESIGN

> Between Dec 2015 and Dec 2020, the GRAAL-2014/B trial

Induction

Consol-1

	QUEST	GRAALL 2014/B
MRD3 neg	72%	53%

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Phase II GMALL-Initial1 trial: Inotuzumab ozogamicin induction followed by standard chemotherapy in older pts with de novo B-lymphoblastic leukemia

Matthias Stelljes, et al. 2022, ASH #212

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STUDY POPULATION AND DESIGN

> Pts aged >55 years with newly diagnosed

OUTCOME

> 45 pts, of whom 43 were evaluable (median age: 64 years; CD22 expression: 69%)

Phase II: Subgroup analysis of ponatinib + blinatumomab for pts with newly-diagnosed Ph-positive ALL

Nicolas Short, et al. 2022, ASH #213

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STUDY POPULATION AND DESIGN

> Pts ≥18 years of age with newly

OUTCOME

> N = 40 (median age: 57 years)

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Advances in Newly Diagnosed ALL

Key Insights

Key Takeaways: Advances in Newly Diagnosed ALL (1/3)

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ALL therapies, excluding transplantation and cellular immunotherapies: Clinical trials

#LBA-1: Consolidation therapy with blinatumomab improves OS in newly diagnosed adult pts with B-

Key Takeaways: Advances in Newly Diagnosed ALL (2/3)

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ALL therapies, excluding transplantation and cellular immunotherapies: Clinical trials (cont.)

#212: Inotuzumab ozogamicin induction followed by standard chemotherapy yields high remission rates and promising survival in

Key Takeaways: Advances in Newly Diagnosed ALL (3/3)

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Management of novel ALL subsets in different age groups

#49: Impact of additional intensive L-asparaginase therapy during consolidation phase for HR ALL: results of a randomized

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Advances in R/R ALL

Conference Highlights From ASH 2022

Phase I: ADCT-602, a CD22-targeting ADC bound to PBD toxin, in adult pts with R/R B-cell ALL

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Nitin Jain, et al. 2022, ASH #216

STUDY POPULATION

> Pts aged ≥18 years with R/R B-ALL and BM blasts ≥5%

DOSING

> ADCT-602 administered IV once Q3W initially, then later

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Phase I: SC blinatumomab in adults with R/R B-cell precursor ALL

Matthias Stelljes, et al. 2022, ASH #2727

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STUDY POPULATION

> Adults with R/R B-cell precursor ALL

DOSING

> 4 cohorts of up to 6 pts each

Any grade CRS: 80%

site reaction, gr3 NTX, POD, etc.)

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Phase I/II: Pembrolizumab + blinatumomab in pts with R/R ALL

Karamjeet S. Sandhu, et al. 2022, ASH #4051

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STUDY POPULATION

> Pts aged ≥18 years with CD19-positive R/R B-ALL

DOSING

> Blinatumomab 9 µg/d on D1–7 and 28 µg/d on D8–28 during C1

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Advances in R/R ALL

Key Insights

Key Takeaways: Advances in R/R ALL

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ALL therapies, excluding transplantation and cellular immunotherapies: Clinical trials

#216: Adct-602, a CD22 targeting ADC bound to PBD toxin in adult pts with R/R B-cell ALL: A phase I trial (Nitin Jain, et al)

APTITUDE HEALTH®

US Headquarters
5901-C Peachtree Dunwoody Road NE
Suite 200, Atlanta, GA 30328, US

EU Headquarters
Wilhelmina van Pruisenweg 104
2595 AN The Hague, the Netherlands

aptitudehealth.com

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