ASH 2022

Pre-Conference Synopsis on CAR-T & TCE Space

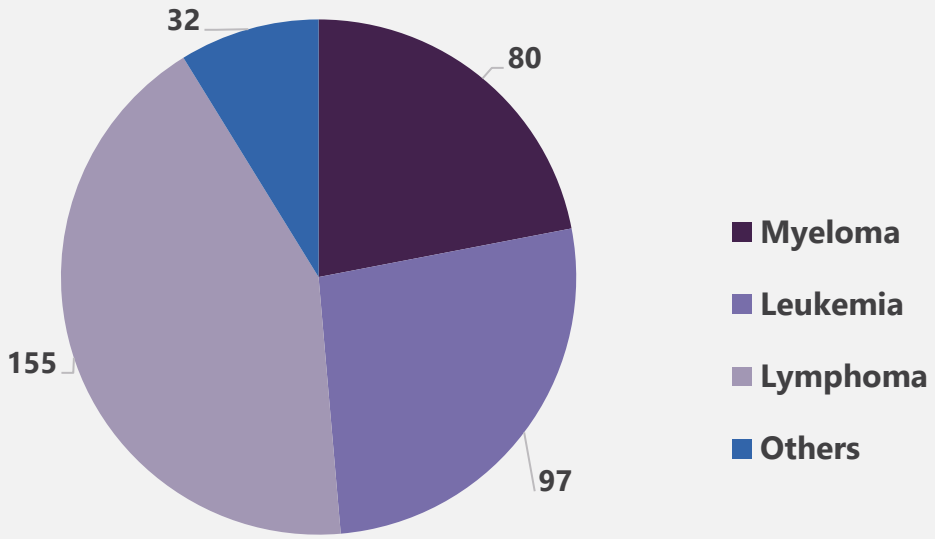
EVALUESERVE

Program Overview on CAR-T & Cell Engagers at ASH'22

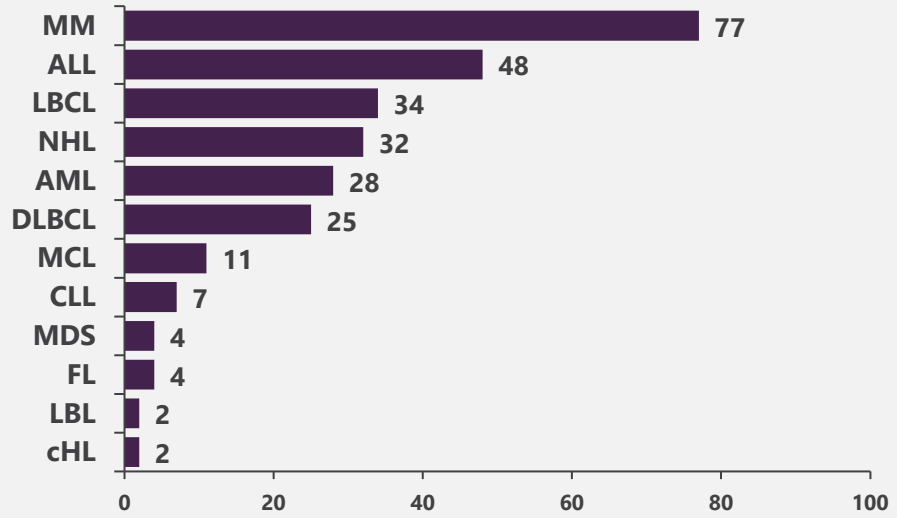
ASH 2022 by Numbers

5200+	280+	40+	9	240+
Total Abstracts	CART Abstracts	TCE Abstracts	Satellite Symposiums & Scientific Programs and Workshops	Posters

Session View by Heme Malignancies



Session View By Indications



Lymphoma-focused CART/TCE sessions are expected to witness maximum presence (~42%) this year, followed by Leukemia (~27%) and Myeloma (~22%)

Note: Others include abstracts focusing on broader hematologic malignancies

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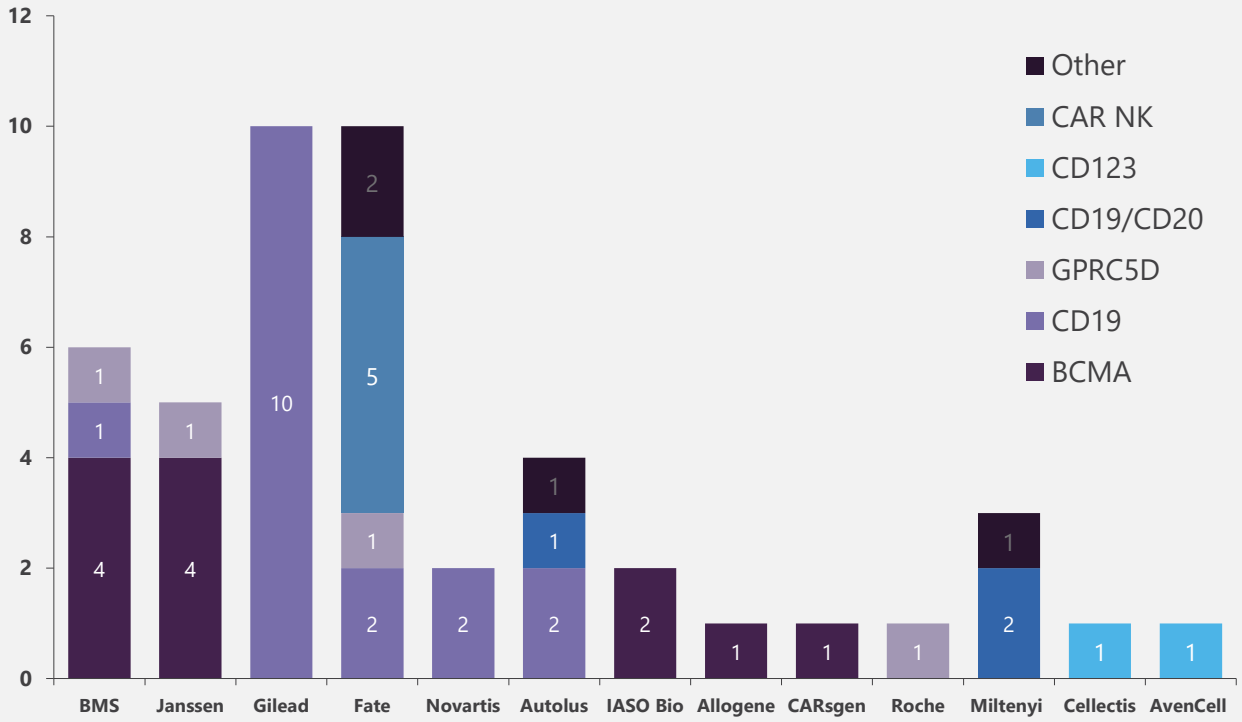
Share of Voice (SoV) by Key Players



Gilead & Fate Therapeutics are the prominent players grabbing highest SOV on data presentations within CAR-T & TCE segment

Topics of Discussion at Speaker Sessions

Poster and oral sessions have maximum traction. Presentations in the **Scientific Workshops** in ASH 2022 focused on CAR-T therapies

- Key focus areas include **evident and emerging toxicities associated with CAR-T therapies** including cytokine release syndrome, Immune effector cell-associated neurotoxicity syndrome, cytopenia etc.

Spotlight Sessions consists of several institute-sponsored sessions

- Major emphasis is anticipated to be on **BiTEs, Immune checkpoint molecules, macrophage checkpoint** molecules and CARTs in AML, MDS and myeloid malignancies

At the ASH 2022, **Special Interest sessions** are institute sponsored and focused also on CAR-T therapies

- Likely presentations and discussions on **CD19+ CAR-T** therapy, current treatment landscape of **BCMA CAR-Ts, CAR-T cells with a 4-1BB** costimulatory domain

Note: Analysis has been done based on the CART/TCE prominent sessions backed by the key pharma companies. Others include all the other CART target such CD38, CD3, ILT3, CD22

What to Expect from CAR-T & TCE segment at ASH'22 ?

Validation of the approved therapies

- Data from in-market BCMA/CD19 therapies are gaining maximum traction this year
- Long-term data from Gilead's Yescarta and Tecartus, a CD19 targeting CART for MCL, LBCL, and MCL is grabbing attention
- BMS will be presenting data from heme portfolio including alnuctamab, BCMA x CD3 TCE, Abecma, BCMA CART and BMS-98639, GPRC5D CART
- Separately, new scoring system developed to predict hematotoxicity in patients on CAR-T, likely to inform better Tx decision making

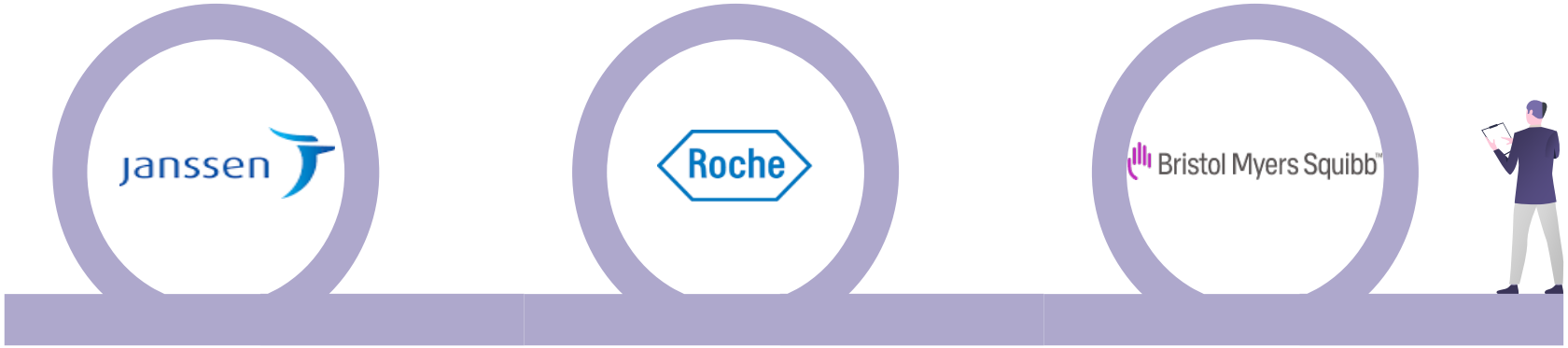
Novel MOA catering unmet need in MM

- BCMA targeted CAR-T therapies have revolutionized the MM treatment. However, frequent relapses are the major hurdles, driving the need for additional multi-antigen targeting and off-the-shelf available therapy.
- GPRC5D expected to emerge as a new therapeutic target for MM
- Will be interesting to observe, how latest data from BMS' BMS-986393, Janssen' talquetamab, and Roche' RG6234 will help unlock potential of GPRC5D in MM
    - Signals of clinical activity observed in early data

Need for next generation CAR-T

- CAR-T cell exhaustion is another major challenge faced by autologous therapies
- Updated data awaited from Caribou Biosciences' CB-010, a next gen CRISPR-edited allogeneic CD19 CAR-T, which could improve the persistence of antitumor activity
    - Recently granted RMAT and FTD
- First data presentation from Gracell's GC012F with dual-target mechanism (BCMA X CD19); likely to yield fast, durable and deep responses in 1L MM
    - FasTCAR platform shortens manufacturing time from 1-6 wks to 22-36 hrs

GPRC5D emerges as a promising immunotherapeutic target in MM within mushrooming BCMA space



157: Talquetamab, a GPRC5D x CD3 TCE in pts with RRMM: Phase 1/2 Results from MonumenTAL-1

- **Talquetamab**, a GPRC5D x CD3 TCE; development ongoing in pts with RRMM
- Readout from Ph 1/2 MonumenTAL-1 study to further validate the potential of GPRC5D and build on the existing encouraging efficacy data reported at ASH'21
- With BTD and PRIME designation in hand, talquetamab seems ahead of its competitors such as Roche's RG6234 and BMS's BMS-986393

161: RG6234, a GPRC5D x CD3 TCE in pts with RRMM: Updated IV and First SC Results from a Ph1 Dose-Escalation study

- **RG6234** is a GPRC5D x CD3 TCE
- First results from Ph1 study in pts with R/R MM demonstrated potential utility of the bispecific antibody
- Subcutaneous data replicates the response showed by earlier IV formulation
- SC formulation could yield edge over in-class competitors, given improved compliance over IV

364: BMS-986393 (CC-95266), a GPRC5D CART in pts with RRMM: First Results from a Ph1, Multicenter, Open-Label Study

- **BMS-986393**, a GPRC5D targeted CART
- Promising preliminary data could further fuel the competition with other GPRC5D agents and support GPRC5D-directed CAR T cell therapy as a new treatment paradigm in RRMM

MM treatment with BCMA-targeted modalities induces high response rates, however relapse is common. A pool of MM cells lacking sufficient BCMA surface expression (antigen escape) may be implicated in relapse. Thus, targeting **GPRC5D may be an effective therapeutic strategy for BCMA Tx -refractory or -relapsed MM patients** to address BCMA escape and potentially confer.

Other Spotlight Sessions (1/3)

3354: CARTITUDE-2 Cohort B data of ciltacabtagene autoleucel in pts with MM

- **Ciltacabtagene autoleucel (Carvykti)**, is a BCMA directed genetically modified autologous CAR-T
- Data in early relapsed multiple myeloma pts- maintained efficacy (ORR of 100% in 19/19 pts, and CR/sCR rate of 90%) with longer follow-up (17.8 months)

159: Elranatamab in pts with RMMM naïve to anti-BCMA therapies: Results from Cohort A of the Magnetismm-3 Study

- **Elranatamab** is a BCMA x CD3 bispecific mAb
- Granted BTD based on potentially pivotal data which demonstrated 61.0% ORR with manageable safety (56.3% CRC, 31.7% Gr3/4 infection)
- Data looks promising, however, superior efficacy outcomes of J&J's Tecvayli (teclistamab), an approved agent, may pose competitive threat despite safety concerns (72% CRS, 45% Gr3/4 infection)

336/3314: Results from cohorts 2a and 2c of the Ph2 KarMMa-2 trial evaluating Abecma in high-risk multiple myeloma

- **Idecabtagene vicleucel (Abecma)** is a BCMA directed genetically modified autologous CAR-T
- Data from cohorts 2a and 2c of the Ph2 KarMMa-2 trial of Abecma support a favorable clinical benefit-risk profile in these patient populations

Other Spotlight Sessions (2/3)

366: Phase I Open-Label Single-Arm Study of GC012F, BCMA/CD19 Dual-Targeting CART as First-Line Therapy for Transplant-Eligible ND High-Risk MM

- **GC012F**, BCMA/CD19 Dual-Targeting CART
- **GC012F demonstrated 100% ORR and 100% MRD negativity in the 13 treated pts** with favorable safety profile, further data required in larger pts pool to validate the initial findings
- With **one day manufacturing**, FasTCAR could significantly improve cell production efficiency, resulting in cost saving and faster access

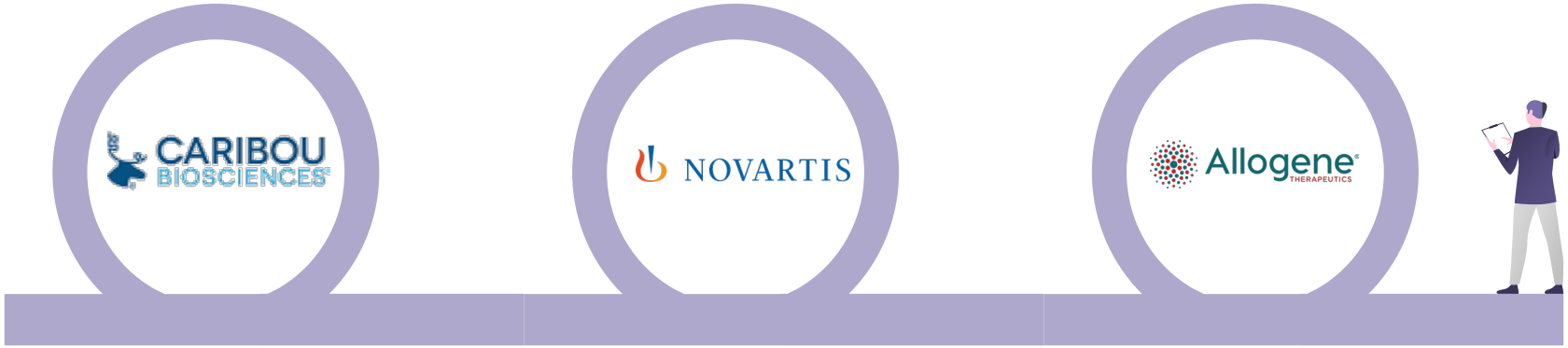
949/444: Odronextamab in pts with R/R FL (Gr 1-3a) and DLBCL: Results from a prespecified analysis of the pivotal Phase II study ELM-2

- **Odronextamab** is a CD20×CD3 bispecific mAb
- First interim data demonstrated compelling efficacy and acceptable safety in both R/R DLBCL and FL.
- With 75% of pts achieving CR by ICR, it could emerge an important treatment option for R/R FL

162: Alnuctamab, a subcutaneous BCMA x CD3 TCE: preliminary results from the dose escalation and expansion R/R MM

- **Alnuctamab**, a BCMA x CD3 TCE
- For heavily pretreated MM pts, ALNUC has demonstrated encouraging activity, however, CRS was a major AEs observed
- Based on promising early efficacy with a low-grade CRS, SC ALNUC comes as alternative to overcome safety issues with IV form

Other Spotlight Sessions (3/3)



4257: CB-010, a next-gen CRISPR-edited allogeneic anti-CD19 CAR-T with a PD-1 knockout in pts with R/R B cell NHL: Results from Ph1 study (ANTLER Study)

- **CB-010** is the **first allogeneic CAR-T with a PD-1 knockout** designed to improve persistence of antitumor activity
- Earlier data showed **100% CR (6/6) best response**, 50% CR (3/6) at 6 month with well tolerated safety, no GvHD or Grade ≥ 2 CRS.
- Special designations, **RMAT for LBCL and FTD for R/R B cell NHL,** will expediate product development and market entry

439: YTB323 (Rapcabtagene Autoleucel, a next gen CD19 CART: follow up data from Phase I Study in R/R DLBCL

- Follow up data from Novartis' **YTB323**, a next generation CD19 CART using **T-Charge platform**, will be interesting as the proprietary technology claims greater proliferative potential and fewer exhausted T-cells compared with traditional CART.

2019: Universal Updated Phase 1 Data Highlights Role of Allogeneic Anti-BCMA ALLO-715 Therapy for R/R MM

- Encouraging responses support continued advancement of **ALLO-715** in R/R multiple myeloma.
- Regulatory discussions planned for potentially pivotal Phase 2 trial

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