Friday, December 9, 2022

Industry Report

China Merchants Securities (HK) Co., Ltd.
Hong Kong Equity Research

China Pharmaceutical & Healthcare

ASH 2022 data readout review

- **ASH 2022 will take place in New Orleans, U.S. on Dec 10-13**
- **BiTEs further advances in MM treatment, novel CAR-T/NK engineering demonstrates new therapeutic merits**
- **We continue to strategically overweight China biotech sector. Top picks BeiGene (BGNE US) for its strong hematology franchise**

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WHAT'S NEW

64th American Society of Hematology updates

Data readout highlights for global pipelines at ASH 2022

Key data readouts：**1) BsAb T-cell engagers (BiTEs) further advances in late line MM:** following recent first MM BiTE of J&J's teclistamab in Oct, BiTEs class further shows advances in r/r MM in this year's ASH. *Pfizer's elranatamab* (BCMA x CD3 BiTE) read ORR at 61% within Ph2 Magnetismm-3 trial (NCT04649359, n=123), *Regeneron's linvoseltamab (REGN5458)* read ORR at 75% within Ph1/2 trial (NCT03761108, n=167), and *J&J's talquetamab* with novel target (GPRC5D x CD3 BsAb) read ORR at 73%, within Ph1/2 MonumenTAL-1 trial (NCT03399799/NCT04634552, n=288). *Amgen/BeiGene's Blinatumomab* (CD3 x CD19 BiTE) demonstrated OS benefits (NR vs. SoC's 71.4mo, HR 0.42, p=0.003) over SoC for 1L ALL (LBA-1). Lastly, Affimed's NK-cell engager AFM13 (CD30 x CD16A BiTE), which precomplexed *in virto* w/ allogeneic NK cells to form a CAR-NK-like features, showed 97% ORR (71% CR) in r/r/ HL. **2) Novel cell therapy catches the eye**: *Novartis's YTB323* (CD19 CAR-T) and *Gracell's GC012F* (BCMA x CD19 Car-T) aim shorten manufacturing time to <2d while maintain competitive clinical profile. In Allogeneic Camp, *Adicet's ADI-001* (CD20 γδ CAR-T) reveals more durability data in lymphoma (7/9 CRs, 1 new relapse). *Fate' FT576* (BCMA CAR-NK) and *CRISPR' CTX110* (CD19 allo CAR-T) showed positive early-phase safety data. Beyond BCMA class, *BMS's BMS-986393* (GPRC5D CAR-T) presented first results from ph1 for pts had prior BCMA therapy (86% ORR and favorable safety). **3) AML race continues:** We noted over 50% abstracts in leukemia segments are studies for AML, o/w majorities are focused on the combinability w/ Ventoclax/azacitidine to make their targeted candidate as a new flexible tool in the AML armamentarium, such as CD47 class (Gliead's magrolimab, ALXO's evopacept), Flt3 (Astellas's gilteritinib) and IDH2 (BMS's enasidenib). Meanwhile, clinical advances in other novel inhibitors in AML continue. *Syndax's revumenib* (ORR=53%) and *Kura's Ziftomenib* (ORR=41.7%), both of which are menin/MLL inhibitors, read positive results among KMT2Ar/NPM1m r/r AML. *Forma's Olutasidenib* (IDH1 inhibitor) for high risk mIDH1 AML.

BeiGene showed strong heme franchise at ASH

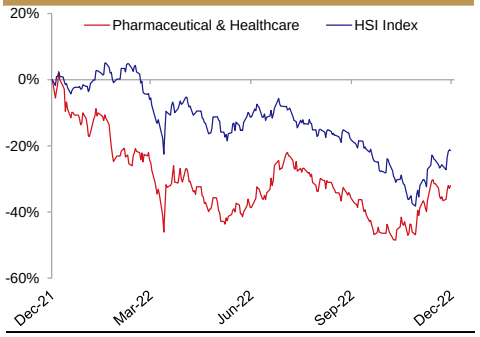
This year, ASH recognized over 80 abstracts from Chinese biotech names, o/w BeiGene accounted for ~20 abstracts of its key hematology pipelines (e.g. zanubrutinib, tislelizumab, BGB-11417 and blinatumomab). Of note, BGNE's zanubrutinib (head-to-head PFS data vs. ibrutinib from ALPINE Ph3 in CLL/SLL) and blinatumomab (OS data from ECOG-ACRIN E1910 ph3) are selected for the two of the six LBAs, reflecting its strong presence in the hematology space.

Investment risk: Clinical failure of clinical assets; Worse than expected data readout; Regulatory delay.

OVERWEIGHT

Previous	OVERWEIGHT
HSI (Dec 9, 2022)	19,901
HSCEI (Dec 9, 2022)	6,834

Sector Performance



Source: Bloomberg

%	1m	6m	12m
Absolute return	5.8	(14.9)	(50.8)
Relative return	(8.9)	(2.6)	(28.3)

Related Research

1. China Pharmaceutical & Healthcare –November data reflects continued funding weakness (OVERWEIGHT) (Dec 09, 2022)
2. China Pharmaceutical & Healthcare – CMS R&D insight 003: CAR-T cell therapies overview (OVERWEIGHT) (Nov 21, 2022)
3. China Pharmaceutical & Healthcare – ESMO 2022 review: rich data readouts within I/O space (OVERWEIGHT) (Sept 20, 2022)
4. China Pharmaceutical & Healthcare – ESMO 2022 preview – KRAS takes centre stage (OVERWEIGHT) (Sept 7, 2022)

Contents

LBA study overview

LBA: frontier R&D movement: ASH 2022 registered six LBA studies with transformative therapeutic benefits or research progress for HC, o/w we noted **Amgen/Beigene's Blinatumomab** (CD3 x CD19 BsAb) offers an opportunity as a new SoC for ALL given significant OS benefits (LBA-1); and **Beigene's Zanubrutinib** (BTKi) shows superiority over first generation BTKi, Ibrutinib, in ORR and PFS readout (LBA-6).

Figure 1: ASH 2022 LBA data readout

No.	Company	Generic name (Brand)	Target	Modalities	Indication	Clinical stage (# of pts)	Trial acronym (NCT ID)	Regimen	ORR (%)	CR (%)	mPFS (mos)	mOS (mos)	Follow-up (mos)	Abstract Title
LBA-1	Amgen/ Astella/ BeiGene	Blinatumomab (Blincyto)	CD3 x CD19	BsAb	1L ALL	Ph3 (n=722)	ECOG-ACRIN E1910 (NCT02003222)			81%		not reached v.s 71 mos	43	Consolidation Therapy with Blinatumomab Improves Overall Survival in Newly Diagnosed Adult Patients with B-Lineage Acute Lymphoblastic Leukemia in Measurable Residual Disease Negative Remission: Results from the ECOG-ACRIN E1910 Randomized Phase III National Cooperative Clinical Trials Network Trial
LBA-2	Novartis	Iptacopan	Factor B	SMD	PNH, Anemia	Ph3 (n=97)	Apply PNH	IPT v.s SoC						Oral Monotherapy with Iptacopan, a Proximal Complement Inhibitor of Factor B, Has Superior Efficacy to Intravenous Terminal Complement Inhibition with Standard of Care Eculizumab or Ravulizumab and Favorable Safety in Patients with Paroxysmal Nocturnal Hemoglobinuria and Residual Anemia: Results from the Randomized, Active-Comparator-Controlled, Open-Label, Multicenter, Phase III Apply-PNH Study
LBA-3	University of Freiburg et al	HDC-ASCT	n.a	Cell therapy	CNS lymphoma	Ph3 (n=260)	MATRix/ IELSG43 (NCT02531841)	Consolidation therapy (HDC-ASCT v.s R-DEVIC)		52%	3 yr PFS: 79% v.s 53%	3 yr OS: 86% v.s 71%	44	Effects on Survival of Non-Myeloablative Chemoimmunotherapy Compared to High-Dose Chemotherapy Followed By Autologous Stem Cell Transplantation (HDC-ASCT) As Consolidation Therapy in Patients with Primary CNS Lymphoma - Results of an International Randomized Phase III Trial (MATRix/IELSG43)
LBA-4	Univeristy of Minnesota	alloHCT	n.a	Cell therapy	GVHD disease relapse	Ph3 (n=128)	BMT CTN 1703	PTCy v.s Tac/MTX			No significant difference			Post-Transplant Cyclophosphamide, Tacrolimus, and Mycophenolate Mofetil As the New Standard for Graft-Versus-Host Disease (GVHD) Prophylaxis in Reduced Intensity Conditioning: Results from Phase III BMT CTN 1703
LBA-5	University of Warwick	Heparin	n.a	SMD	R/R ALIFE2	Ph3 (n=428)		LMWH v.s SoC	live birth rate: 71.6% v.s 70.9%					Low-Molecular-Weight Heparin Versus Standard Pregnancy Care for Women with Recurrent Miscarriage and Inherited Thrombophilia (ALIFE2): An Open-Label, Phase III Randomized Controlled Trial (confex.com)
LBA-6	BeiGene	Zanubrutinib (Brukinsa)	BTK	SMD	R/R CLL/SLL	Ph3 (n=652)	ALPINE (NCT03734016)	Zanu v.s Ibru	86.2 vs 75.7%, P=0.0007		NR vs. 35mo P=0.0024		29.6	Zanubrutinib Demonstrates Superior Progression-Free Survival (PFS) Compared with Ibrutinib for Treatment of Relapsed/Refractory Chronic Lymphocytic Leukemia and Small Lymphocytic Lymphoma (R/R CLL/SLL): Results from Final Analysis of ALPINE Randomized Phase 3 Study

Sources: CMS (HK), ASH 2022

Multiple Myeloma – study overview

MM frontier R&D movement: **1) BsAb further advances:** post FDA's approval of Johnson & Johnson's teclistamab on 25th Oct 2022 based on MajesTEC-1 trial (n=165, NCT03145181/NCT04557098, ORR= 62%), BsAb further shows advances in r/r MM. o/w we noted the following assets showed good readouts: *Pfizer's elranatamab* (BCMA x CD3 BsAb) read ORR at 61% within Ph2 Magnetismm-3 trial (NCT04649359, n=123), *Regeneron's linvoseltamab* read ORR at 75% within Ph1/2 trial (NCT03761108, n=167), and *JOHNSON's alquetamab* with novel target (GPRC5D x CD3 BsAb) read ORR at 73%, within Ph1/2 MonumenTAL-1 trial (NCT03399799/NCT04634552, n=288). **2) CAR-NK shows early merits:** beyond BCMA targeting CAR-T therapies, we noted *Fate therapeutics' FT576* offers 'off-shelf' potential as generated from renewable pluripotent stem cell line. Within the Ph1 trial, no CRS, NT or GvHD were reported at two dosing regiments (100m or 300m cells/dose). Despite at early stage, NK cells show next R&D wave of cancer therapy given advantages of availability (i.e. multiple sources from iPSC, NK cell lines) and safety profile[1-2]. **3) GPRC5D as novel target:** class C group 5 member D (GPRC5D) protein have been shown to express on CD138+ MM cells from primary marrow samples in a BCMA independent manner[3]. We noted early stage trials show promising results from this novel target, o/w and *JOHNSON's alquetamab* with novel target (GPRC5D x CD3 BsAb) read ORR at 73%, within Ph1/2 MonumenTAL-1 trial (NCT03399799/NCT04634552, n=288). *Bristol Myers Squibb's BMS-986393*, GPRC5D targeting CAR-T, read high efficacy (ORR at 86%) in 14 pts. What's more, pts had prior line of BCMA targeted therapies (i.e. 4/5 for mAb, 3/5 for CAR-T) also showed response. **4) CD38 mAb centers early line treatment:** *J&J's daratumumab*, current SoC for 1L MM per NCNN guideline, read ORR at 89% within Ph3 IFM2017-03 trial (n=259, NCT03993912). Besides, we noted *Sanofi's isatuximab* read impressive ORR at 100% for SMM within Ph3 ITHACA trial (n=23).

Figure 2: ASH 2022 data readout – Multiple Myeloma

Company	Generic name	Target	Modality	Phase	Indication	ORR (%), Others	CR (%)	Trial Acronym	Enrolment	NCT ID	Abstract Title
GSK, Seagen	belantamab mafodotin	BCMA	ADC	Ph 2	1L MM	ORR: 82.1%		GEM-BELA-VRd	40	NCT04802356	Belantamab Mafodotin in Combination with Vrd for the Treatment of Newly Diagnosed Transplant Eligible Multiple Myeloma Patients: Results from the Phase II, Open Label, Multicenter, GEM-BELA-Vrd Trial
CARsgen	zevorcabtagene autoleucel	BCMA	CAR-T	Ph 2	r/r MM	ORR: 92.8%	CR/sCR: 42.2%	LUMMICAR STUDY 1	102	NCT03975907	Phase II Study of Fully Human BCMA-Targeting CAR-T Cells (Zevorcabtagene Autoleucel) in Patients with Relapsed/Refractory Multiple Myeloma
BMS, Celgene	idecabtagene vicleucel	BCMA	CAR-T	Ph 2	MM	ORR: 83.8%	CR: 45.9%	KarMMa-2	39	NCT03601078	KarMMa-2 Cohort 2a: Efficacy and Safety of Idecabtagene Vicleucel in Clinical High-Risk Multiple Myeloma Patients with Early Relapse after Frontline Autologous Stem Cell Transplantation
BMS, Celgene	idecabtagene vicleucel	BCMA	CAR-T	Ph 2	MM	ORR: 87.1%		KarMMa-2	32	NCT03601078	KarMMa-2 Cohort 2c: Efficacy and Safety of Idecabtagene Vicleucel in Patients with Clinical High-Risk Multiple Myeloma Due to Inadequate Response to Frontline Autologous Stem Cell Transplantation
Fate therapeutics	FT579	BCMA	CAR-NK	Ph 1	r/r MM	* No G3 CRS, NT	n.a	n.a	9	n.a	Interim Phase I Clinical Data of FT576 As Monotherapy and in Combination with Daratumumab in Subjects with Relapsed/Refractory Multiple Myeloma

Company	Generic name	Target	Modality	Phase	Indication	ORR (%), Others	CR (%)	Trial Acronym	Enrolment	NCT ID	Abstract Title
Allogene	ALLO-715	BCMA	CAR-T	Ph 1	>3L r/r MM	ORR: 80%	CR: 27%	UNIVERSAL	53	NCT04093596	Universal Updated Phase 1 Data Highlights Role of Allogeneic Anti-BCMA ALLO-715 Therapy for Relapsed/Refractory Multiple Myeloma
Arcellx	CART-Ddbcma	BCMA	CAR-T	Ph 1	r/r MM	ORR: 100%	CR: 71%	n.a	37	n.a	Phase 1 Study of CART-Ddbcma for the Treatment of Subjects with Relapsed and /or Refractory Multiple Myeloma
Gracell	GC012F	BCMA	CAR-T	Ph 1	1L MM	ORR: 100%	CR: 69%	n.a	13	NCT04935580	Phase I Open-Label Single-Arm Study of BCMA/CD19 Dual-Targeting FasTCAR-T Cells (GC012F) As First-Line Therapy for Transplant-Eligible Newly Diagnosed High-Risk Multiple Myeloma
Pfizer	elranatamab	BCMA x CD3	BsAb	Ph 2	r/r MM	ORR: 61%	n.a	Magnetismm-3	123	NCT04649359	Efficacy and Safety of Elranatamab in Patients with Relapsed/Refractory Multiple Myeloma Naïve to B-Cell Maturation Antigen (BCMA)-Directed Therapies: Results from Cohort a of the Magnetismm-3 Study
Regeneron	linvoseltamab	BCMA x CD3	BsAb	Ph 1/2	r/r MM	ORR: 75%	n.a	n.a	167	NCT03761108	Updated Safety and Efficacy of REGN5458, a BCMAxCD3 Bispecific Antibody, Treatment for Relapsed/Refractory Multiple Myeloma: A Phase 1/2 First-in-Human Study
Abbive	HPN217	BCMA x CD3 x albumin	TsAb	Ph 1	r/r MM	*No G3 CRS	n.a	n.a	49	NCT04184050	Updated Interim Results from a Phase 1 Study of HPN217, a Half-Life Extended Tri-Specific T Cell Activating Construct (TriTAC®) Targeting B Cell Maturation Antigen (BCMA) for Relapsed/Refractory Multiple Myeloma (RRMM)
Pfizer	elranatamab	BCMA x CD3	BsAb	Ph 3	r/r MM			Magnetismm-5	28	NCT05020236	Elranatamab in Combination with Daratumumab for Patients (pts) with Relapsed/Refractory Multiple Myeloma (RRMM): Results from the Phase 3 Magnetismm-5 Study Safety Lead-in Cohort
Johnson & Johnson	daratumumab	CD38	mAb	Ph 2	r/r MM	ORR: 60%		Dedalo	45	NCT04124497	Dedalo: Phase II Study of Daratumumab Plus Pomalidomide and Dexamethasone (DPd) in Patients with Relapsed/Refractory Multiple Myeloma and 17p Deletion
Sanofi	isatuximab	CD38	mAb	Ph 3	SMM	ORR: 100%	CR: 30.4%	ITHACA	23	NCT04270409	Isatuximab in Combination with Lenalidomide and Dexamethasone in Patients with High-Risk Smoldering Multiple Myeloma: Updated Safety Run-in Results from the Randomized Phase 3 Ithaca Study
Johnson & Johnson	daratumumab	CD38	mAb	Ph 3	1L MM	ORR: 68%		MAXDARA	24	NCT03792620	Daratumumab (Dara), Cyclophosphamide, Thalidomide and Dexamethasone for Transplant Eligible Newly Diagnosed Multiple Myeloma (TE NDMM) Patients: Response Rate Impacts on PFS
Johnson & Johnson	daratumumab	CD38	mAb	Ph 3	1L MM	ORR: 89% vs. 77%		IFM2017-03	295	NCT03993912	A Dexamethasone Sparing-Regimen with Daratumumab and Lenalidomide in Frail Patients with Newly-Diagnosed Multiple Myeloma: Efficacy and Safety Analysis of the Phase 3 IFM2017-03 Trial

Company	Generic name	Target	Modality	Phase	Indication	ORR (%), Others	CR (%)	Trial Acronym	Enrolment	NCT ID	Abstract Title
Johnson & Johnson	daratumumab	CD38	mAb	Ph 2	1L MM	ORR: 95%			25	NCT04151667	Daratumumab Based Response Adapted Therapy for Older Adults with Newly Diagnosed Multiple Myeloma: Interim Analysis of Phase II Study
J&J, Takerda	daratumumab; ixazomib	CD38	mAb, SMD	Ph 2	2L MM	ORR: 83%			37	NCT03590652	Phase II Study of the Combination of Daratumumab, Ixazomib, Pomalidomide, and Dexamethasone in Early Relapsed/Refractory Multiple Myeloma
Sanofi	isatuximab	CD38	mAb	Ph 2	1L MM	ORR: 100%		SKylaRk	50	NCT04430894	A Phase II Study of Once Weekly Carfilzomib, Lenalidomide, Dexamethasone, and Isatuximab in Newly Diagnosed, Transplant-Eligible Multiple Myeloma (The SKylaRk Trial)
Bristol Myers Squibb	BMS-986393	GPRC5D	CAR-T	Ph 1	r/r MM	ORR: 86%	n.a	n.a	21	NCT04674813	Clinical Activity of BMS-986393 (CC-95266), a G Protein–Coupled Receptor Class C Group 5 Member D (GPRC5D)–Targeted Chimeric Antigen Receptor (CAR) T Cell Therapy, in Patients with Relapsed and/or Refractory (R/R) Multiple Myeloma (MM): First Results from a Phase 1, Multicenter, Open-Label Study
Johnson & Johnson	Talquetamab	GPRC5D x CD3	BsAb	Ph 1/2	r/r MM	ORR: 73%	CR: 29%	Monumen TAL-1	288	NCT03399799/ NCT04634552	Talquetamab, a G Protein-Coupled Receptor Family C Group 5 Member D x CD3 Bispecific Antibody, in Patients with Relapsed/Refractory Multiple Myeloma (RRMM): Phase 1/2 Results from MonumenTAL-1
Takeda	ixazomib	protease	SMD	Ph 2	MM	ORR: 65% vs 42%		IRB00077 815	42	NCT02765854	Phase II Trial of Ixazomib and Dexamethasone Versus Ixazomib, Dexamethasone and Lenalidomide, Randomized with NFKB2 Rearrangement. (Proteasome Inhibitor NFKB2 Rearrangement Driven Trial, PINR)
Roche	RG6234	GPRC5D xCD3	BsAb	Ph 1	r/r MM	*G3 CRS IV: 2%; SC: 1.9%	n.a	n.a	51	NCT04557150	RG6234, a GPRC5DxCD3 T-Cell Engaging Bispecific Antibody, Is Highly Active in Patients (pts) with Relapsed/Refractory Multiple Myeloma (RRMM): Updated Intravenous (IV) and First Subcutaneous (SC) Results from a Phase I Dose-Escalation Study
Celgene, BMS	mezigdomide	IKZF3, IKZF1, CRBN	SMD	Ph 2	r/r MM	ORR: 39.6%		CC-92480-MM-001	101	NCT03374085	Mezigdomide (CC-92480), a Potent, Novel Cereblon E3 Ligase Modulator (CELMoD), Combined with Dexamethasone (DEX) in Patients (pts) with Relapsed/Refractory Multiple Myeloma (RRMM): Preliminary Results from the Dose-Expansion Phase of the CC-92480-MM-001 Trial
Beigene	carfilzomib; daratumumab	Protease, CD38	mAb	Ph 2	1L MM	n.a	CR/sCR: 65.2%	n.a	30	NCT04113018	Interim Results of a Risk-Adaptive Phase II Study: Carfilzomib, Lenalidomide, Dexamethasone and Daratumumab (KRD-Dara) in Newly Diagnosed Multiple Myeloma (NDMM) at the Levine Cancer Institute (LCI)

Sources: CMS (HK), ASH 2022, Grey, key study to watch

Leukemia – study overview

Leukemia frontier R&D movement: 1) Addressing KMT2Ar/NPM1m genotying*:* The presence of KMT2Ar and NPM1m (i.e. KMT2A rearrangement, NPM1 mutation) occurs in ~5-10% and ~30% of AML, and drives leukemognesis. Targeted inhibition of menin disrupts KMT2A associated protein complex, thus proving it rational to treat r/r AML with KMT2Ar/NPM1m[5-6]. We noted *Syndax's revumenib* (ORR=53%) and *Kura's Ziftomenib* (ORR=41.7%) read positive results among KMT2Ar/NPM1m r/r AML. Other drug candidate that addresses mutated AML also include *BMS' azacitidine* (DNMT, DNA methyltransferase inhibitor) for KMT2Ar r/r AML, and *Forma's Olutasidenib* (IDH1 inhibitor) for high risk mIDH1 AML, as well as *Novartis's ruxolitinib* (JAK1/2 inhibitor) for CRLF2r Ph-like ALL. **2) I/O therapeutics across early to late line treatment**, except for ADCs (e.g. Pfizer's CD22 ADC Besponsa) moves onto 1L ALL, and expected high efficacy readout from CAR-T therapies (e.g JW Therapeutics' relma-cel) for 3L MCL, Astellas/Amgen/Beigene's CD3 x CD19 BsAb read rich data from two Ph3 trials (NCT04994717, NCT02003222) showing efficacy and survival benefits for 1L ALL.

Figure 3: ASH 2022 data readout – Leukaemia

Company	Generic name	Target	Modality	Phase	Indication	ORR (%)	CR (%)	mPFS, mOS (month)	Trial Acronym	Enrolment	NCT ID	Abstract Title
Hansoh	flumatinib	Bcr-Abl	SMD	Ph 2	1L ALL		CR: 93.2%		RJ-ALL2020.2A	44	ChiCTR2100042248	A Phase II Study of Flumatinib with Chemotherapy for Newly Diagnosed Ph/BCR-ABL1-Positive Acute Lymphoblastic Leukemia in Adults : Preliminary Results from RJ-ALL2020.2A Trial
Pfizer	inotuzumab ozogamicin	CD22	ADC	Ph 2	1L ALL		CR/CRp: 90%		EWALL-INO	131	NCT03249870	Fractionated Inotuzumab Ozogamicin Combined with Low-Intensity Chemotherapy in Older Patients with Newly Diagnosed CD22+ Philadelphia Chromosome (Ph)-Negative B-Cell Precursor (BCP) Acute Lymphoblastic Leukemia (ALL): Results of the EWALL-INO Study
Amgen/ Astellas/ BeiGene	blinatumomab	CD3 x CD19	BsAb	Ph 3	1L PH-ve ALL		CR: 100%			10	NCT04994717	Blinatumomab Alternating With Low-Intensity Chemotherapy (CT) Treatment for Older Adults With Newly Diagnosed Philadelphia (Ph)-Negative B-Cell Precursor Acute Lymphoblastic Leukemia (BCP-ALL) is Well Tolerated and Efficacious: Safety Run-In Results for the Phase 3 Randomized Controlled Golden Gate Study
Amgen/ Astellas/ BeiGene	blinatumomab	CD3 x CD19	BsAb	Ph 2	PH-ve ALL	CMR 80%;			Blina-CELL	29	NCT04554485	Single Cycle of Blinatumomab Followed By High-Dose Chemotherapy in the Induction Therapy for Ph-Negative Acute Lymphoblastic Leukemia in Adults. Primary Endpoint Analysis of the Blina-Cell Trial
BMS	azacitidine	DNMT	SMD	Ph 2	1L ALL			3-year EFS: 34.2%	AALL15P1	56	NCT02828358	A Pilot Study of Azacitidine As Epigenetic Priming for Chemotherapy in Infants Less Than 1 Year of Age with KMT2A-Rearranged Acute Lymphoblastic Leukemia (ALL); Results from the Children's Oncology Group (COG) Trial AALL15P1
Novartis	ruxolitinib	JAK1/2	SMD	Ph 2	ALL		MRD-negative: 44.4%		AALL1521/INCB18424-269	23	NCT02723994	A Phase 2 Study of Ruxolitinib with Chemotherapy in Children with Philadelphia Chromosome-like Acute Lymphoblastic Leukemia (AALL1521/INCB18424-269): Biologic Characteristics and Minimal Residual Disease Response of Patients with Non-CRLF2-Rearranged JAK Pathway Alterations

Company	Generic name	Target	Modality	Phase	Indication	ORR (%)	CR (%)	mPFS, mOS (month)	Trial Acronym	Enrolment	NCT ID	Abstract Title
Pfizer	inotuzumab ozogamicin	CD22	ADC	Ph 2	ALL			MRD negativity: 35%	ALL2418	39	NCT03610438	Gimema ALL2418: Interim Analysis of a Phase IIa Study of Feasibility and Effectiveness of Inotuzumab Ozogamicin in Adult Patients with B-Cell Acute Lymphoblastic Leukemia with Positive Minimal Residual Disease before Any Hematopoietic Stem Cell Transplantation
Pfizer	inotuzumab ozogamicin	CD22	ADC	Ph 2	ALL	MRD-67%				27	NCT03441061	A Phase II Study of Inotuzumab Ozogamicin for the Treatment of Measurable Residual Disease-Positive B-Cell Acute Lymphoblastic Leukemia
Pfizer	inotuzumab ozogamicin	CD22	ADC	Ph 2	1L ALL		CR/CRi: 100%	1-year EFS: 88%	INITIAL-1	45	NCT03460522	Inotuzumab Ozogamicin Induction Followed By Standard Chemotherapy Yields High Remission Rates and Promising Survival in Older (>55 Years) Patients with De Novo B-Lymphoblastic Leukemia (GMALL-Initial1 Trial)
Juventas, CASI	inaticabtagene autoleucel	CD19	CAR-T	Ph 2	R/R ALL		CR/CRi: 65.6%		HY001201	53	NCT04684147	Sustained Remission and Decreased Severity of CAR T-Cell Related Adverse Events: A Pivotal Study Report of CNCT19 (inaticabtagene autoleucel) Treatment in Adult Patients with Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-Cell ALL) in China
Beijing Boren Hospital	donor-derived CAR T	CD19	CAR-T	Ph 2	ALL	ORR: 90%			BR-IIT-LCYJ-2020-005	20	NCT04689659	Efficacy and Safety of Donor-Derived CD7 CAR T Cells for r/r T-Cell Acute Lymphoblastic Leukemia/Lymphoma: Interim Analysis from a Phase 2 Trial
Sainofi, Merck	clofarabine; mitoxantrone	DNA, TOP II	SMD, RNAi	Ph 2	R/R ALL, AML		MRD negative CR: 88%			39	NCT01842672	Final Results of Phase I/II Trial of Mitoxantrone in Combination with Clofarabine (MITCL) in Children with Relapsed/Refractory Acute Leukemia
Roche, Abbvie	venetoclax	BCL-2	SMD	Ph 2	ALL, AML		CR/CRi (AML): 28.6%; CR/CRi (ph- B-cell ALL): 55.6%		SZRRAL01	30	NCT05190549	Venetoclax, Cladribine Plus Low-Dose Cytarabine Achieved High Remission in Patients with Relapse/Refractory Acute Leukemia: Preliminary Results of a Phase II Study
Astellas	blinatumomab ; ponatinib	CD3 x CD19, BCr-Abl	BsAb, SMD	Ph 2	R/R ALL, CML		CMR: 69%			16		A Phase II Study of the Sequential Combination of Low-Intensity Chemotherapy (mini-hyper-CVD) and Ponatinib Followed By Blinatumomab and Ponatinib in Patients with Philadelphia Chromosome-Positive (Ph+) Acute Lymphoblastic Leukemia (ALL)
Roche, Abbvie	venetoclax	BCL-2	SMD	Ph 2	AML		CR/CRi: 77%			22	ACTRN12619000746134	A Prospective Phase 2 Study of Venetoclax and Low Dose Ara-C (VALDAC) to Target Rising Molecular Measurable Residual Disease and Early Relapse in Acute Myeloid Leukemia
Roche, Abbvie	venetoclax	BCL-2	SMD	Ph 2	AML		MRD response: 68%			25	ACTRN12619000746134	A Prospective Phase 2 Study of Venetoclax and Low Dose Ara-C (VALDAC) to Target Rising Molecular Measurable Residual Disease and Early Relapse in Acute Myeloid Leukemia
DCprime	DCP-001	n.a	vaccine	Ph 2	Maintenance AML			MRD response: 35%	ADVANCE-II	20	NCT03697707	Use of an Allogeneic Leukemia-Derived Dendritic Cell Vaccine in MRD+ AML-Patients Results in MRD Conversion, Improved Relapse-Free Survival and Vaccine Induced Immune Responses to Tumor Antigens

Company	Generic name	Target	Modality	Phase	Indication	ORR (%)	CR (%)	mPFS, mOS (month)	Trial Acronym	Enrolment	NCT ID	Abstract Title
Roche, Abbvie	venetoclax	BCL-2	SMD	Ph 2	R/R AML	ORR: 60%	CRc: 53%			33		Updated Phase IIb Results of Venetoclax with FLAG-IDA in Relapsed or Refractory Acute Myeloid Leukemia
Ocular therapeutix	dexamethasone	Glucocorticoid	Corticoid	Ph 2	1L AML		CR/CRi: 83.3%		DEXAML-02	120	NCT03609060	Dexaml-02: A Phase II Study of Dexamethasone Added to Induction and Postremission Therapy in Older Patients with Newly Diagnosed AML. a French Innovative Leukemia Organization (FILO) Study
Pfizer	cytarabine	DNA	SMD	Ph 2/3	1L AML			3-year EFS: 61.2% vs 64.3% (p=0.551)	JPLSG-AML-12	359	jRCTs041180128	Evaluation of High-Dose Cytarabine Induction Therapy and Flow Cytometric Measurable Residual Disease Monitoring for Children with De Novo Acute Myeloid Leukemia: A Report from the JPLSG-AML-12 Trial
BMS	azacitidine	DNMT	SMD	Ph 2	1L AML				ZDYYGZ201912	20	NCT04248595	Azacitidine Combined with Homoharringtonine, Idarubicin/ Daunorubicin, Cytarabine for Previously Untreated Patients with Acute Myeloid Leukemia: A Single-Center, Phase 2 Study
n.a	azacitidine;tamibarotene;venetoclax	DNMT, BCL-2	SMD, SMD	Ph 2	1L AML		CR/CRi: 100%		SELECT-AML-1	6	NCT04905407	Initial Results from SELECT-AML-1, a Phase 2 Study of Tamibarotene in Combination with Venetoclax and Azacitidine in RARA-Positive Newly Diagnosed AML Patients Ineligible for Standard Induction Chemotherapy
Novo Nordisk	olutasidenib	IDH1	SMD	Ph 2	R/R AML	ORR: 48%	CR/CRh/ CRi: 45%;		FT2102-HEM-101	153	NCT02719574	Olutasidenib (FT-2102) Induces Durable Complete Remissions in Patients with Relapsed/Refractory mIDH1 Acute Myeloid Leukemia. Results from a Planned Interim Analysis of a Phase 2 Pivotal Clinical Trial
BMS	nivolumab	PD-1	mAb	Ph 2	Maintenance AML			mPFS: 13.2 vs 10.9 months	REMAIN	79	NCT02275533	Randomized Phase II Study to Assess the Role of Nivolumab As Single Agent to Eliminate Minimal Residual Disease and Maintain Remission in Acute Myelogenous Leukemia (AML) Patients after Chemotherapy (NCI9706 protocol; REMAIN Trial)
Gilead	entospletinib	Syk	SMD	Ph 2	1L AML		CR/CRh/ CRi: 78%		BAML-16-001	30	NCT03013998	Entospletinib (ENTO) in Combination with Cytarabine (Ara-C) and Daunorubicin (DNR) in Newly Diagnosed (ND) Adult Patients with NPM1-Mutated and FLT3-ITD Wild-Type Acute Myeloid Leukemia (AML) Is Associated with Good Response and Survival: A Phase 2 Sub-Study of the Beat AML Master Trial
Kura Oncology	ziftomenib	MLL	SMD	Ph 1/2	R/R AML	ORR: 41.7%	CRc: 33.3%	n.a	n.a	30	n.a	Update on a Phase 1/2 First-in-Human Study of the Menin-KMT2A (MLL) Inhibitor Ziftomenib (KO-539) in Patients with Relapsed or Refractory Acute Myeloid Leukemia
Syndax	SNDX-5613	MLL	SMD	Ph 1	R/R AML	ORR 53%	CR 38%	n.a	AUGMENY-101	68	NCT04065399	Outcomes after Transplant in Relapsed/Refractory KMT2Ar (MLLr) and mNPM1 (NPM1c) leukemia Patients Achieving Remissions after Menin Inhibition: SNDX-5613 (revumenib) Ph1 Experience
Aptose Biosciene	HM43239	FLT3/SYK	SMD	Ph 1/2	n.a	16% ORR,	7/50 CRs		n.a	n.a	n.a	A Phase 1/2 Dose Escalation Study of the Myeloid Kinase Inhibitor HM43239 in Patients with Relapsed or Refractory Acute Myeloid Leukemia
Curis	n.a	Irak-4	SMD	Ph 1/2	n.a	n.a	n.a		n.a	n.a	n.a	Molecular Characterization of Clinical Response in Relapsed/Refractory Acute Myeloid Leukemia and High-Risk Myelodysplastic Syndrome Patients Treated with Single Agent Emavusertib

Company	Generic name	Target	Modality	Phase	Indication	ORR (%)	CR (%)	mPFS, mOS (month)	Trial Acronym	Enrolment	NCT ID	Abstract Title
GSK, Novartis	eltrombopag	TPO	SMD	Ph 2	AML, CIT		platelet transfusions: 9.76 vs 12.56		EPAG 2015	110	NCT03603795	Epag 2015 : A Phase II Randomized Placebo-Controlled Study to Assess the Impact on Outcome of Eltrombopag Administered to Elderly Patients with Acute Myeloid Leukemia Receiving Induction Chemotherapy. a French Innovative Leukemia Organization (FILO) Study
Roche, Abbvie	ponatinib; venetoclax	Bcr-Abl T3151, BCL-2	BTK, BCL-2	Ph 2	R/R AML, CML	ORR: 75%	CR/CRi: 33%			12	NCT04188405	A Phase II Study of the Combination of Decitabine, Venetoclax and Ponatinib in Patients with Chronic Myeloid Leukemia (CML) in Myeloid Blast Phase (MBP) or Philadelphia-Chromosome Positive (Ph+) Acute Myeloid Leukemia (AML)
Celgene, BMS	CC-486 (oral azacitidine)	protease	SMD	Ph 2	AML, CMML, MDS				2018-01-AZA	40	NCT03493646	In Vivo Drug Incorporation and Intracellular Dynamics of Injectable Versus Oral Azacytidine: A Phase II Open Label Multicentre Trial
BMS	azacitidine	DNMT	SMD	Ph 2	AML, HSCT, MDS, MPD			4-year OS: 36%		39	NCT02497404	Epigenetic Priming with 5-Azacytidine Prior to Allogeneic Stem Cell Transplantation for Myeloid Malignancies with In Vivo T Cell Depletion: Results of a Phase II Trial
Pfizer, UCB	gemtuzumab ozogamicin	CD33	ADC	Ph 2/3	AML, MDS		CR/CRi: 67.3%		NCRI AML18	844	NCT02272478	A Randomized Comparison of the Fractionated Versus Single Dose Schedule of Gemtuzumab Ozogamicin at Induction with Determinants of Benefit for Older AML Patients: UK NCRI AML18 Trial Results
Immuneel therapeutics	varnimcabtagene autoleucel	CD19	CAR-T	Ph 2	R/R B-cell malignancies	ORR: 100%			IMAGINE	8	CTRI/2022/03/041162	Response, Peak and Persistence of Varnimcabtagene Autoleucel (IMN-003A), First-in-India Industry CD19-Directed CAR-T Cell Therapy, with Fractionated Infusions for Patients with Relapsed and/or Refractory B Cell Malignancies: Early Results (IMAGINE Study)
Baylor	ADI-001	CD20	CAR-T	Ph 1	R/R lymphomas	ORR: 78%	n.a		n.a	11	n.a	A Phase 1 Study of ADI-001: Anti-CD20 CAR-Engineered Allogeneic Gamma Delta1 (γδ) T Cells in Adults with B-Cell Malignancies
Astrazeneca	acalabrutinib	BTK	SMD	Ph 2	1L CLL	ORR: 100%	CR: 52%			31	NCT03580928	Updated Results from a Multicenter, Phase 2 Study of Acalabrutinib, Venetoclax, Obinutuzumab (AVO) in a Population of Previously Untreated Patients with CLL Enriched for High-Risk Disease
Roche, Abbvie	ibrutinib; venetoclax	BTK, BCL-2	SMD, SMD	Ph 2	1L CLL	MRD <0.01%: 63.8% vs 61.3%			Filo	120		Preliminary Results of the Filo Phase 2 Trial for Untreated Fit Patients with Intermediate Risk Chronic Lymphocytic Leukemia Comparing Ibrutinib Plus Venetoclax (IV) Versus FCR: Results of the Month 15 MRD Evaluation
n.a	ibrutinib; obinutuzumab; venetoclax	BTK, CD20, BCL-2	SMD, SMD	Ph 2	1L CLL		CR: 58.5%		CLL2-GIVe	41	NCT02758665	Final Analysis of the Prospective Multicenter CLL2-Give Trial of Obinutuzumab (GA101, G), Ibrutinib (I), and Venetoclax (Ve) in Untreated Patients with CLL with 17p Deletion/TP53 Mutation
Johnson & Johnson	daratumumab	CD38	mAb	Ph 2	R/R CLL	ORR: 78%			IDA53	29	NCT03734198	Combined Treatment with Ibrutinib and Anti-CD38 Monoclonal Antibody Daratumumab in Relapsed/Refractory Chronic Lymphocytic Leukemia with TP53 Aberrations: Results of the Filo Phase II Study IDA53
Merck	nemtabrutinib	BTK C481S	SMD	Ph 2	3L CLL, SLL	ORR: 56%			BELLWAVE-001	57	NCT03162536	Efficacy and Safety of Nemtabrutinib, a Wild-Type and C481S-Mutated Bruton Tyrosine Kinase Inhibitor for B-Cell Malignancies: Updated Analysis of the Open-Label Phase 1/2 Dose-Expansion Bellwave-001 Study

Company	Generic name	Target	Modality	Phase	Indication	ORR (%)	CR (%)	mPFS, mOS (month)	Trial Acronym	Enrolment	NCT ID	Abstract Title
n.a	ibrutinib; venetoclax	BTK, BCL-2	SMD, SMD	Ph 2	1L CLL, SLL	ORR: 100%			HOVON 158/Next STEP	30	NCT04639362	Exploratory Results of PET-CT and Residual Lymph Node Fine Needle Aspiration of Patients Treated with First-Line Venetoclax and Ibrutinib for CLL/Sll; First Interim Analysis of the Phase 2 HOVON 158/Next STEP Trial
Norvatis	asciminib	STAMP	SMD	Ph 2	Add-On CML	deep molecular response: 28.6% vs 0% vs 4.8%			ASC4MORE	84	NCT03578367	Efficacy and Safety Results from ASC4MORE, a Randomized Study of Asciminib (ASC) Add-on to Imatinib (IMA), Continued IMA, or Switch to Nilotinib (NIL) in Patients (Pts) with Chronic-Phase Chronic Myeloid Leukemia (CML-CP) Not Achieving Deep Molecular Responses (DMRs) with ≥1 Year of IMA
	cobimetinib			Ph 2	CMML	ORR: 50%			Concerto	6	NCT04409639	Concerto (NCT04409639): A Phase 2 Trial of Cobimetinib in Newly Diagnosed and HMA-Treated CMML Patients with RAS Pathway Mutations
Novartis	ruxolitinib	JAK1/2	SMD	Ph 2	CMML	ORR: 17%			MCC-19727	29	NCT03722407	Efficacy and Safety of Ruxolitinib for Treatment of Symptomatic Chronic Myelomonocytic Leukemia (CMML): Results of a Multicenter Phase II Clinical Trial

Sources: CMS (HK); ASH 2022, Grey, key study to watch

Lymphoma – study overview

Lymphoma frontier R&D movement: Except from rich data readouts from BTKi, we noted *Affimed's FIC cell engager* (CD30 x CD16 BsAb) that selectively bridges NK (natural killing) cells (CD16+) and tumour cells (CD30+) for tumor lysis function reads high efficacy within Ph1/2 trial (NCT04074746, n=30), ORR was at 97%, CR at 63%.

Figure 4: ASH 2022 data readout – Lymphoma

Company	Generic name	Target	Modality	Phase	Indication	ORR (%), Others	CR (%)	Trial Acronym	Enrolment	NCT ID	Abstract Title
Merck	nemtabrutinib	BTK C481S	SMD	Ph 2	3L CLL, SLL	ORR: 56%		BELLWAVE-001	57	NCT03162536	Efficacy and Safety of Nemtabrutinib, a Wild-Type and C481S-Mutated Bruton Tyrosine Kinase Inhibitor for B-Cell Malignancies: Updated Analysis of the Open-Label Phase 1/2 Dose-Expansion Bellwave-001 Study
AbbVie	ibrutinib; venetoclax	BTK, BCL-2	SMD, SMD	Ph 2	1L CLL, SLL	ORR: 100%		HOVON 158/Next STEP	30	NCT04639362	Exploratory Results of PET-CT and Residual Lymph Node Fine Needle Aspiration of Patients Treated with First-Line Venetoclax and Ibrutinib for CLL/Sll; First Interim Analysis of the Phase 2 HOVON 158/Next STEP Trial
Beigene	zanubrutinib	BTK	SMD	Ph 2	1L DLBCL	ORR: 94%			17		Efficacy and Safety of Zanubrutinib Combined with R-CHOP Regimen in the Treatment of Newly Diagnosed Diffuse Large B-Cell Lymphoma with Extranodal Involvement: A Single-Arm, Prospective Phase II Trial
Beigene	zanubrutinib	BTK	SMD	Ph 2	1L DLBCL	ORR: 93%			46		Zanubrutinib PLUS RCHOP(ZR-CHOP) Regimen Achieves High Complete Response Rate in the Treatment of Newly-Diagnosed Double-Expression Diffuse Large B Cell Lymphoma
Beigene	zanubrutinib	BTK	SMD	Ph 2	1L DLBCL		CR: 83.3%	HNSZLYYNHL05	14	NCT04668365	Preliminary Results of a Phase Ⅱ Study of Zanubrutinib Combined with Immunochemotherapy in Patients with CD79A/CD79B-Mutant Diffuse Large B-Cell Lymphoma
AstraZeneca	acalabrutinib	BTK	SMD	Ph 2	2L DLBCL	ORR: 74%; CR: 53%		ESR-LY-808-SCI	19	NCT03736616	Initial Efficacy and Safety of Acalabrutinib Plus RICE in Transplant Eligible Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma
Regeneron	odronextamab	CD3 x CD20	BsAb	Ph 2	3L DLBCL	ORR: 53%		ELM-2	121	NCT03888105	Odronextamab in Patients with Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL): Results from a Prespecified Analysis of the Pivotal Phase II Study ELM-2
BMS	lenalidomide	multi	molecular glue	Ph 2	1L DLBCL	ORR: 95%		DE-LYM2019	67	NCT04164368	Preliminary Result of Lenalidomide Combined with R-CHOP(R2-CHOP) in Newly Diagnosed Double-Expressor Diffuse Large B-Cell Lymphoma: A Prospective Phase II Clinical Trial
Roche, Seagen	polatuzumab vedotin	CD79b	mAb	Ph 2	2L DLBCL	ORR: 92%			41	NCT04665765	Polatuzumab Vedotin Combined with R-ICE (PolaR-ICE) As Second-Line Therapy in Relapsed/Refractory Diffuse Large B-Cell Lymphoma
BMS, Novartis, Beigene	orelabrutinib; tislelizumab	BTK, PD-1	SMD, mAb	Ph 2	R/R DLBCL	ORR: 87.5%	CR: 25.0%		0	ChiCTR2200056256	Efficacy and Safety of Lenalidomide, Anti-PD-1 Antibody Combined with Orelabrutinib or Rituximab in the Treatment of Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma
Junshi	toripalimab	PD-1	mAb	Ph 2	1L DLBCL	ORR: 100%	CR: 87.5%	TREND	37	NCT04058470	Combination Anti-PD1 Antibody and Rituximab Followed By R-CHOP for Elderly Patients with Newly Diagnosed DLBCL: Analysis of the Phase II TREND Trial

Company	Generic name	Target	Modality	Phase	Indication	ORR (%), Others	CR (%)	Trial Acronym	Enrolment	NCT ID	Abstract Title
Regeneron	Odronextamab	CD20×CD3	BsAb	Ph 2	r/r DLBCL	ORR: 53%	CR: 37%	ELM-2	121	NCT03888105	Odronextamab in Patients with Relapsed/Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL): Results from a Prespecified Analysis of the Pivotal Phase II Study ELM-2
Norvatis	Rapcabtagene Autoleucel	CD19	CAR-T	Ph 1	r/r DLBCL	n.a	CR: 65%	n.a	45	NCT03960840	YTB323 (Rapcabtagene Autoleucel) Demonstrates Durable Efficacy and a Manageable Safety Profile in Patients with Relapsed/Refractory Diffuse Large B-Cell Lymphoma: Phase I Study Update
Crisper therapeutics	CTX110	CD19	CAR-T	Ph1	r/r LBCL	ORR: 67%	CR: 41%	CARBON	34	NCT04035434	CTX110 Allogeneic CRISPR-Cas9–Engineered CAR T Cells in Patients (Pts) with Relapsed or Refractory (R/R) Large B-Cell Lymphoma (LBCL): Results from the Phase 1 Dose Escalation Carbon Study
Astellas, Eisai	bendamustine	DNA	SMD	Ph 2	DLBCL, FL, MCL		primary endpoint: 19.5% vs 20.9%		108	NCT02278796	A Randomized Phase II Trial Comparing BeEAM with BEAM As Conditioning Regimen for Autologous Stem Cell Transplantation in Lymphoma Patients
Regeneron, Zai Lab	odronextamab	CD3 x CD20	BsAb	Ph 2	3L FL	ORR: 81%		ELM-2	96	NCT03888105	Odronextamab in Patients with Relapsed/Refractory (R/R) Follicular Lymphoma (FL) Grade 1–3a: Results from a Prespecified Analysis of the Pivotal Phase II Study ELM-2
Baylor, UNC, Tessa	TT11	CD30	CAR-T	Ph 2	R/R HL	ORR: 73.3%		CHARIOT	15	NCT04268706	Updated Results and Correlative Analysis: Autologous CD30.CAR-T-Cell Therapy in Patients with Relapsed or Refractory Classical Hodgkin Lymphoma (CHARIOT Trial)
Seagen	brentuximab vedotin; nivolumab	CD30, PD-1	ADC	Ph 2	HL	ORR: 93%	CR: 88%	SGN35-027	58	NCT03646123	Brentuximab Vedotin, Nivolumab, Doxorubicin, and Dacarbazine (AN+AD) for Advanced Stage Classic Hodgkin Lymphoma: Updated Efficacy and Safety Results from the Single-Arm Phase 2 Study (SGN35-027 Part B)
CrystalGenomics	camrelizumab	PD-1	mAb	Ph 2	1L HL	ORR: 100%	CR: 88.2%;		20		Phase II Clinical Trial of Camrelizumab Combined with AVD (Epirubicin, Vincristine and Dacarbazine) in the First-Line Treatment for Patients with Advanced Classical Hodgkin's Lymphoma
Affimed	AFM13	CD30	BsAb - NK cells	Ph 1/2	R/R lymphomas	ORR: 97%	CR: 63%	n.a	30	NCT04074746	Innate Cell Engager AFM13 Combined with Preactivated and Expanded Cord Blood-Derived NK Cells for Patients with Double Refractory CD30+ Lymphoma
Fosun kite, Daichi Sankyo	axicabtagene ciloleucel	CD19	CAR-T	Ph 2	2L LBCL			ALYCANTE	43	NCT04531046	Axicabtagene Ciloleucel As Second-Line Therapy for Large B-Cell Lymphoma in Transplant-Ineligible Patients: Primary Analysis of Alycante, a Phase 2 Lysa Study
CRISPR Therapeutics	CTX110	CD19	CAR-T	Ph1	n.a	ORR: 67%	CR: 41%	n.a	n.a	n.a	CTX110 Allogeneic CRISPR-Cas9–Engineered CAR T Cells in Patients (Pts) with Relapsed or Refractory (R/R) Large B-Cell Lymphoma (LBCL): Results from the Phase 1 Dose Escalation Carbon Study
Autolus	AUTO4	TRBC1	CAR-T	Ph 1	n.a	ORR: 9/73	CR: 5/73	n.a	73	NCT03590574	First in Human Study of AUTO4, a TRBC1-Targeting CAR T-Cell Therapy in Relapsed/Refractory TRBC1-Positive Peripheral T-Cell Lymphoma
Pfizer	doxycycline	30S subunit	SMD	Ph 2	1L MALT lymphoma	ORR: 64%		IELSG39	44	NCT01820910	Six-Month Doxycycline Is Safe and Effective As Upfront Monotherapy for Stage-I Malt Lymphoma of the Ocular Adnexae: Primary Endpoint Results of the IELSG39 Trial
Roche	CD19 4-1BBL	CD19	BsAb	Ph 1		ORR: 67%	CR: 73%	n.a	70	NCT04077723	CD19 4-1BBL (RO7227166) a Novel Costimulatory Bispecific Antibody Can be Safely Combined with the T-Cell-Engaging Bispecific Antibody Glofitamab in Relapsed or Refractory B-Cell Non-Hodgkin Lymphoma

Company	Generic name	Target	Modality	Phase	Indication	ORR (%), Others	CR (%)	Trial Acronym	Enrolment	NCT ID	Abstract Title
Xencor	Plamotamab	CD20×CD3	BsAb	Ph 1		ORR: 47.4%	CR: 30.8%	n.a	36	NCT02924402	A Phase 1 Study of Plamotamab, an Anti-CD20 x Anti-CD3 Bispecific Antibody, in Patients with Relapsed/Refractory Non-Hodgkin's Lymphoma: Recommended Dose Safety/Efficacy Update and Escalation Exposure-Response Analysis
Merck	pembrolizumab	PD-1	mAb	Ph 2	3L NKTCL, LBCL, PMBCL	ORR: 28%	CR: 23%		17	NCT03210662	Phase II Study of Pembrolizumab and Fractionated External Beam Radiotherapy in Patients with Relapsed and Refractory Large B-Cell Lymphoma
Beigene	zanubrutinib	BTK	SMD	Ph 2	1L WM	ORR: 100%;		BDH-WM2020/04	20	NCT04463953	Zanubrutinib Plus Ixazomib and Dexamethasone for Newly Diagnosed Symptomatic Waldenström Macroglobulinemia: A Prospective, Phase II Study
Merck	pembrolizumab	PD-1	mAb	Ph 2	R/R WM	ORR: 47.1%		Pembrowm	17	NCT03630042	Pembrowm: Results of a Multi-Centre Phase II Trial Investigating the Safety and Efficacy of Rituximab and Pembrolizumab in Relapsed/Refractory Waldenström's Macroglobulinaemia

Sources: CMS (HK); ASH 2022, Grey, key study to watch

Novel therapeutic technology– CAR-T therapy overview

CAR-T therapy frontier R&D movement: 1) Data readouts show high efficacy: we noted CAR-T therapies continue to demonstrate high efficacy in r/r HC hematology, o/w **J&J/Legend Bio's BCMA CAR-T** ciltacabtagene autoleucel read high efficacy for R/R MM (ORR=100%) within CARTIFAN-1 trial. Besides, the CARTIFAN-1 data readouts showed fair benefit-risk profile for late-line MM pts. At 26.4 median fellow-up for late line (≥4L) MM pts, ORR read at 85.4%, CR at 79.2%. 24-month PFS and OS rates were 52.6% and 74.2% respectively. **2) Novel CAR-T engineering demonstrates therapeutic merit:** novel CAR-T engineering technologies showcase potential of overcoming current safety or availability limitations, o/w we noted *Adicet's ADI-001* (CD20 γδ CAR-T) for B-cell malignancies demonstrated good efficacy (ORR at 78%, and CR at 78%), without G3 GvHD risk, and no G3 GRS, or NT reports. Besides, CRISPR therapeutics showcase Allogeneic (allo) CAR T engineering ability by deploying CRISPR/Cas9 based system (ORR at 67%, CR at 41%), no G3 CRS, and 2/32 G3 NT reports.

Figure 5: ASH 2022 data readout – CAR-T therapies

Company	Generic name	Target	Modality	Phase	Indication	ORR (%)	CR (%)	mPFS/mOS (months) / Others	Trial Acronym	Enrolment	NCT ID	Abstract Title
Immuneel therapeutics	varnimcabtagene autoleucel	CD19	CAR-T	R/R B-cell malignancies	R/R Ph 2	ORR: 100%			IMAGINE	8	CTRI/2022/03/041162	Response, Peak and Persistence of Varnimcabtagene Autoleucel (IMN-003A), First-in-India Industry CD19-Directed CAR-T Cell Therapy, with Fractionated Infusions for Patients with Relapsed and/or Refractory B Cell Malignancies: Early Results (IMAGINE Study)
J&J, Legend	ciltacabtagene autoleucel	BCMA	CAR-T	R/R MM		ORR 85.4%	CR 75%	PFS: NR, 24 mos: 52.6%	CARTIFAN-1	48		Phase 2, Open-Label Study of Ciltacabtagene Autoleucel, an Anti-BCMA CAR-T Cell Therapy, in Chinese Patients with Relapsed/Refractory Multiple Myeloma (CARTIFAN-1): 26-Month Median Follow-up
J&J, Legend	ciltacabtagene autoleucel	BCMA	CAR-T	R/R MM		ORR 100%	CR >90%		CARTITUDE-2	19		Ciltacabtagene Autoleucel (Cilta-cel), a BCMA-Directed CAR-T Cell Therapy, in Patients with Multiple Myeloma (MM) and Early Relapse after Initial Therapy: CARTITUDE-2 Cohort B 18-Month Follow-up
Fosun kite, Daichi Sankyo	axicabtagene ciloleucel	CD19	CAR-T	2L LBCL	Ph 2			CMR: 67.5%	ALYCANTE	43	NCT04531046	Axicabtagene Ciloleucel As Second-Line Therapy for Large B-Cell Lymphoma in Transplant-Ineligible Patients: Primary Analysis of Alycante, a Phase 2 Lysa Study
JW theraputics	relmacabtagene autoleucel	CD19	CAR-T	3L R/R MCL	Ph 2	ORR: 72.7%	CR: 54.5%		JWCAR029-005	35	NCT04718883	Preliminary Safety and Efficacy of Relmacabtagene Autoleucel (relma-cel) in Adults with Relapsed/Refractory Mantle Cell Lymphoma (r/r MCL) in China
Baylor, UNC, Tessa	TT11	CD30	CAR-T	R/R HL	Ph 2	ORR: 73.3%			CHARIOT	15	NCT04268706	Updated Results and Correlative Analysis: Autologous CD30.CAR-T-Cell Therapy in Patients with Relapsed or Refractory Classical Hodgkin Lymphoma (CHARIOT Trial)
Juventas, CASI	inaticabtagene autoleucel	CD19	CAR-T	R/R B-cell ALL	Ph 2		CR/CRi: 65.6%		HY001201	53	NCT04684147	Sustained Remission and Decreased Severity of CAR T-Cell Related Adverse Events: A Pivotal Study Report of CNCT19 (inaticabtagene autoleucel) Treatment in Adult Patients with Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-Cell ALL) in China
CARsgen	zevorcabtagene autoleucel	BCMA	CAR-T	R/R MM	Ph 2	ORR: 92.8%	CR/sCR: 42.2%		LUMMICAR STUDY 1	102	NCT03975907	Phase Ⅱ Study of Fully Human BCMA-Targeting CAR-T Cells (Zevorcabtagene Autoleucel) in Patients with Relapsed/Refractory Multiple Myeloma

Company	Generic name	Target	Modality	Phase	Indication	ORR (%)	CR (%)	mPFS/mOS (months) / Others	Trial Acronym	Enrolment	NCT ID	Abstract Title
Beijing Boren Hospital	donor-derived CAR T	CD19	CAR-T	T-cell ALL	Ph 2	ORR: 90%			BR-IIT-LCYJ-2020-005	20	NCT04689659	Efficacy and Safety of Donor-Derived CD7 CAR T Cells for r/r T-Cell Acute Lymphoblastic Leukemia/Lymphoma: Interim Analysis from a Phase 2 Trial
Adicet	γδ CAR-T	CD20	γδ CAR-T	B cell malignancies	Ph 1	ORR: 78%	CR: 78%		n.a	11	n.a	A Phase 1 Study of ADI-001: Anti-CD20 CAR-Engineered Allogeneic Gamma Delta1 (γδ) T Cells in Adults with B-Cell Malignancies
Crisper therapeutics	CTX110	CD19	CAR-T	DLBCL	Ph1	ORR: 67%	CR: 41%	n.a	CARBON	34	NCT04035434	CTX110 Allogeneic CRISPR-Cas9–Engineered CAR T Cells in Patients (Pts) with Relapsed or Refractory (R/R) Large B-Cell Lymphoma (LBCL): Results from the Phase 1 Dose Escalation Carbon Study
Novartis	ibrutinib; tisagenlecleucel	BTK, CD19	SMD, CAR-T	R/R MCL	Ph 2	ORR: 90%	CR: 80%		TARMAC	21	NCT04234061	Time-Limited Ibrutinib and Tisagenlecleucel Is Highly Effective in the Treatment of Patients with Relapsed or Refractory Mantle Cell Lymphoma, Including Those with TP53 Mutated and Btki-Refractory Disease: First Report of the Tarmac Study
BMS	idecabtagene vicleucel	BCMA	CAR-T	MM	Ph 2	ORR: 83.8%	CR: 45.9%		KarMMa-2	39	NCT03601078	KarMMa-2 Cohort 2a: Efficacy and Safety of Idecabtagene Vicleucel in Clinical High-Risk Multiple Myeloma Patients with Early Relapse after Frontline Autologous Stem Cell Transplantation

Sources: CMS (HK); ASH 2022; Grey, key study to watch

Appendix A: FDA approvals for hematological malignancies

Among 35 FDA approved products from 2020 to 2022, we noted MM (11/30) and AML (4/30) as top focus by indication, and CAR-T therapies (9/35) mark as new technology trend. At ASH 2022, we noted impressive data readouts that highlight transformative therapeutic potential to fill unmet medical needs.

Appendix A: FDA approvals for haematological malignancies (2020 – 2022)

Approval Date	Company	Generic name	Trade name	Target	Modality	Indications	Trial name	NCT No.	Trial size	ORR (%)	CR (%)	PFS (mos)	OS (mos)	Commmon AE
18 Dec 2022	Karyopharm	selinexor	XPOVIO	XPO1	SMD	2/3L r/r MM	BOSTON	NCT03110562	402	n.a	n.a	13.9 (v.s 9.5)	n.a	G3 AE >10% thrombocytopenia, lymphopenia
25 Oct 2022	Janssen	teclistamab-cqyv	Tecvayi	BCMA x CD3	BsAb	4L r/r MM	MajesTEC-1	NCT03145181; NCT04557098	165	63.0	39.4	11.3	n.a	CRS: 88% G3 0.6%; NT: 81% G3 26%
11 Oct 2022	Seagen	brentuximab vedotin	Adecetris	CD30	ADC	1L cHL	AHOD1331	NCT02166463	600	n.a	n.a	3-yr EFS: 92.1% (vs 82.5%)	n.a	> G3 AE 5%: neutropenia, anemia
26 Aug 2022	Incyte	pemigatinib	Pemaztte	FGFR1/2/3	SMD	2L r/r FGFR1+ve MM	FIGHT-203	NCT03011372	28	n.a	73.7%, CCyR 70%	n.a	n.a	CRS: 79%
24 Jun 2022	BMS	lisocabtagene maraleucel	Breyanzi, liso-cel	CD19	CAR-T	2L LBCL	TRANSFORM	NCT03575351	184	n.a	n.a.	mEFS 10.1 (vs. 2.3)	n.a	CRS: 45% G3 1.3%; NT: 27% G3 7%
27 May 2022	Norvatis	tisagenlecleucel	Kymriah	CD20	CAR-T	3L+ r/r FL	ELARA	NCT03568461	98	86	69	n.a	n.a	>20% AE CRS, infection, fatigue
25 May 2022	Agios/CStone	ivosidenib	Tibsovo	IDH1, DNMT	SMD, SMD	1L AML	AGILE	NCT03173248	146	n.a	47	12m EFS: 37% (v.s 12%)	24.0 (vs 7.9)	diarrhea 25%
1 Apr 2022	Fosun kite, Daiichi Sankyo	axicabtagene ciloleucel	Yescarta	CD19	CAR-T	2L LBCL	ZUMA-7	NCT03391466	359	83 % (vs. 50%)	65% (vs. 32%)	mEFS 8.3 (vs. 2.0)	n.a	CRS: 90% G3 9%; NT: 78% G3 25%
28 Feb 2022	Janssen, Lengend bio	ciltacabtagene autoleucel	Carvykti	BCMA	CAR-T	>4L r/r MM	CARTITUDE-1	NCT03548207	97	97%	67%	mDOR 21.8m	n.a	≥G3 CRS 5%
12 Jan 2022	Rigel Pharma	olutasidenib	n.a	IDH1	SMD	r/r AML	2102-HEM-101	NCT02719574	147	48%	CR/CRh/CRi: 45%;	mDOR 25.9m	n.a.	AE: nausea 20%
29 Oct 2021	Novartis	asciminib	Scemblix	STAMP	SMD	>2L r/r CML	ASCEMBL	NCT03106779	233	24 wk MMR 25% (vs. 13%)	n.a	n.a	n.a	Lower discontinuation 7% (vs. 25%); Infection 20%
14 Sep 2021	BeiGene	zanubrutinib	Brukinsa	BTK	SMD	2L MZL	MAGNOLIA, BGB-3111-AU-003	NCT03846427, NCT02343120	66	56%, 80%	20%, 20%	mDOR NR (vs. 8.3%m), 12m DoR 72%	n.a	> 30% AE: neutrophil, infection, platelet count
23 Apr 2021	ADC Theraputics	loncastuximab tesirine-lpyl	Zynlonta	CD19	ADC	3L LBCL	LOTIS-2	NCT03589469	145	48.3%	24.1%	mDoR 10.3m	n.a	>20% neutropenia, anemia

Approval Date	Company	Generic name	Trade name	Target	Modality	Indications	Trial name	NCT No.	Trial size	ORR (%)	CR (%)	PFS (mos)	OS (mos)	Commmon AE
31 Mar 2021	Sanofi	isatuximab	Sarclisa	CD38	mAb	2L+ r/r MM	IKEMA	NCT03275285	302	86.6% (vs. 82.9%)	39.7% (vs 39.7%)	NR (vs. 19.2m)	n.a	> 20% AE: infection, fatigue et al
26 Mar 2021	Abcam, BMS	idecabtagene vicleucel	Abecma	BCMA	CAR-T	>4L R/R MM	KarMMa	NCT03601078	127	72%	28%	mDoR 11m	n.a	CRS 85% (≥G3 CRS 9%)
5 Mar 2021	Kite Pharma	axicabtagene ciloleucel	Yescarta	CD19	CAR-T	2L+ r/r FL	ZUMA-5	NCT03105336	146	92%	76%	mDoR NR (vs. 14.5m)	n.a	≥G3 CRS 8%
26 Feb 2021	Oncopeptides	melphalan flufenamide	Pepaxto	DNA	SMD	2L r/r MM	HORIZON	NCT02963493	97	23.7%	n.a	mDoR 4.2m	n.a	> 20% AE: infection, fatigue et al
5 Feb 2021	BMS	lisocabtagene maraleucel	Breyanzi	CD19	CAR-T	r/r MM	TRANSCEND	NCT02631044	192	73%	54%	mDoR 16.7m	n.a	CRS 46% (≥G3 CRS 4%)
5 Feb 2021	TG Therapeutics	umbralisib	Ukoniq	PI3K	SMD	2L r/r MZL	UTX-TGR-205	NCT02793583	69	49%	16%	mDoR NR	n.a	> 18% SAE
10 Jan 2021	Kite Pharma	brexucabtagene autoleucel	Tecartus, Brexu-cel	CD19	CAR-T	r/r ALL	ZUMA-3	NCT02614066	54	n.a	65%			G3 CRS: 3.26%; G3 NT: 35%
9 Jan 2021	BeiGene	zanubrutinib	Brukinsa	BTK	SMD	WM	ASPEN	NCT03053440	201	78% (vs. 78%)	n.a	n.a	n.a	n.a
16 Oct 2020	AbbVie, Genetech	venetoclax	Venclexta	BCL-2	SMD	1L AML	VIALE-A, VIALE-C	NCT02993523, NCT03069352	286	n.a	37% (vs. 18%)	n.a	14.7m (vs. 9.6m); 7.2m (vs. 4.1m, p=0.11)	nausea 30%
14 Oct 2020	Merck	pembrolizumab	Keytruda	PD-1	mAb	2L+ r/r cHL	KEYNOTE-204	NCT02684292	304	66% (vs. 54%)	25% (vs. 24%)	13.2m (vs. 8.3m)	n.a	Permanent discontinuation 14%
20 Aug 2020	Jassen	daratumumab	Darzalex	CD38	mAb	2/3L r/r MM	CANDOR	NCT03158688	466	85%	n.a	28.6m (vs 15.2m)	n.a	> 20% AE: infection, fatigue et al
5 Aug 2020	GSK	belantamab mafodotin	Blenrep	BCMA	ADC	>4L r/r MM	DREAMM-2	NCT 03525678	n.a	32%	n.a	mDoR 11m	13.7m	> 20% AE: keratopathy, visual acuity
31 Jul 2020	MorphoSys/ Innocare	tafasitamab	MONJUVI	CD19	mAb	2L r/r DLBCL	L-MIND	NCT02399085	81	55	37	mDoR 21.7m	n.a	neutropenia 20%
24 Jul 2020	Gilead	brexucabtagene autoleucel	Tecartus	CD19	CAR-T	r/r MCL	ZUMA-2	NCT02601313	74	87%	62%	n.a	n.a	≥G3 CRS 18%, ≥G3 NT 37%
22 Jun 2020	Karyopharm	selinexor	XPOVIO	XPO1	SMD	3L r/r DLBCL	SADAL	NCT02227251	134	29%	13%	n.a	n.a	thrombocytopenia 15%
18 Jun 2020	Epizyme/ HCM	tazemetostat	Tazverik	EZH2	SMD	2L r/r FL	E7438-G000-101	NCT01897571	42	69%/34%	12%/4%	mDoR 13m	n.a	>20% AE fatigue, infection, nausea
16 Jun 2020	Wyeth Pharma	gemtuzumab ozogamicin	MYLOTARG	CD33	mAb	1L AML	AAML0531	NCT00372593	1,063	n.a	n.a.	EFS HR 0.84	3yr OS 69.4% (vs. 65.4%, p=0.39)	G3 infection 5%

Sources: CMS (HK); FDA

Appendix B: NCCN recommended treatment in hematology

Appendix B1: NCCN recommended treatment options for NHL

NHL subtype	Incidence rate in US (per 100k)	5 yr Survival rate	NCCN recommended 1L treatments	NCCN recommended 2L+ treatments	New trend & Clinical progress
CLL/SLL	**3.9**	**87.5%**	**1. CD20 mAB** Rituxan / Gazyva + Chemo **2. BTK inhibitors** Ibrutinib, zanubrutinib, acalabrutinib Acalabrutinib +/- Gazvya **3. BCl-2 inhibitor** Venetoclax + Gazvya	**1. CD20 mAb** Rituxan / Gazvya / Arzarra + Chemo **2. BTK inhibitors** Ibrutinib / Acalabrutinib **3. PI3K inhibitors** Duvelisib; Idelalisib + Rituxan **4. BCl-2 inhibitor** Venetoclax + Rituxan **5. Others** Lenalidomide, Ofatumumab, Alemtuzumab (CD52)+ Rituxan	• BTK inhibitor combos (BCL-2, CD38, JAK, RO1, ATR, PI3K) • PI3K + CD20
DLBCL	**5.6**	**64.6%**	**1. CD20 mAB** Rituxan-CHOP	**1. CD 19 mAb /CAR-T** Yescarta / Kymriah，tafasitamab **2. CD20 mAB** Rituxan + Chemo **3. CD79b ADC** Polatuzumab vedotin-piiq	• CD20 + CD3 bsAB • CD79b + BR • PI3K + CD20 • CD19 CAR-T • CD30 ADC (Brentuximab vedotin) • BTK inhibitor (inbrutinib for non-GCB DLBCL)
FL	**2.6**	**90.2%**	**1. CD20 mAB** Rituxan / Gazvya + Chemo	**1. CD20 mAB** Rituxan / Gazvya + Chemo **2. PI3K inhibitors** Zydelig / Aliqopa	• CD20 + CD3 bsAB • PI3K + CD20
MZL	**-**	**-**	**1. CD20 mAB** Rituxan + Chemo	**1. BTK inhibitor** Ibrutinib	• PI3K + CD20
MCL	**-**	**-**	**1. CD20 mAB** Rituxan + Chemo	**1. BTK inhibitor** Ibrutinib / Acalabrutinib / Zanubrutinib **2. UE3 ligase** Lenalidomide	• CD19 CAR-T
WM	**-**	**-**	**1. CD20 mAB + BTK** Ibrutinib + Rituxan	**1. BTK inhibitor** Ibrutinib	-

Sources: CMS (HK); NCNN guideline, 5-year survival 2012-2018

Appendix B2: NCCN recommended treatment options for Leukemia

Leukemia	Incidence rate in US (per 100k)	5 yr Survival rate	1L Treatment	2L+ Treatment	New trend & clinical progress
ALL	**1.8**	**70.8%**	**1. Bcr-abl L TKi + chemo** e.g ponatinib/dasatinib/bosutinib + chemo **2. TKi + corticosteroid**	**1. Tki +/- CD-19 mAb** e.g Tki + Blinatumomab **2. Tki + chemo/corticosteroid** **3. auto-SCT** **4. CD22 ADC** e.g CD22 ADC - Inotuzumab ozogamicin +/- bosutinib **5. CAR-T therapy** e.g CD19 CAR-T - Tisagenlecleucel (Kymriah) **6. Tki + chemo** e.g. BCL-2 inhibitor Venetoclax + chemo	• BsAb (CD3 x cD19), • JAK1/2, DNMT inhibitor, CD-19 CAR-T
CLL	**4.1**	**87.9%**	**1. BTKi** e.g Zanubrutinib, Ibrutinib **2. BTKi + CD20 mAb** e.g Acalabrutinib + obinutuzumab **3. BCL-2 + CD20 mAb** e.g Venetoclax + Obinutuzumab **4. CD20 mAb + chemo** e.g rituximab + Bendamustine **5. CD20 mAb + CD52 mAb** e.g rituximab +/- Alemtuzumab	**1. BTKi** e.g Zanubrutinib, Ibrutinib **2. BCL-2 inhibitor + CD20 mAb** e.g Venetoclax + rituximab **3. PI3K inhibitor + CD20 mAb** e.g Idelalisib + rituximab (e.g Duvelisib) **4. CD20 mAb + chemo** e.g rituximab + Bendamustine	• PD-1 • DNMT, IDH1 inhibitor,
AML	**4.1**	**30.5%**	**1. Chemo** e.g cytarabine **2. CD33 ADC + chemo** e.g gemtuzumab + chemo **3. BCL-2 + LDAC** e.g. venetoclax + azacitidine **4. Flt3** e.g. Gilteritinib **5. IDH1/2** e.g. Enasidenib (IDH2), ivosidenib (IDH1)	**1. Chemo** e.g cytarabine - high dose, Etoposide + cytarabine **2. CD33 ADC + chemo** e.g gemtuzumab + chemo **3. auto-SCT**	• BCL-2 inhibitor • KMT2A, DNMT inhibitor, • CD33 ADC
CML	**1.8**	**70.4%**	**1, CD20 mAb + chemo** e.g. Rituximab + CHOP/Bendamustine	**1. BTKi** e.g Zanubrutinib, Ibrutinib **2. BTKi + CD20 mAb + chemo** e.g Ibrutinib + rituximab + lenalidomide **3. BCL-2 inhibitor + CD20 mAb** e.g Venetoclax + rituximab **4. BCL-2 inhibitor + BTKi** e.g Venetoclax + ibrutinib **5. allo-SCT** **6. CD19 CAR-T** e.g brexucabtagene autoleucel (Tecartus)	• CD19 CAR-T

Sources: CMS (HK); NCCN guideline，5-year survival 2012-2018

Appendix B3: NCCN recommended treatment options for Myeloma

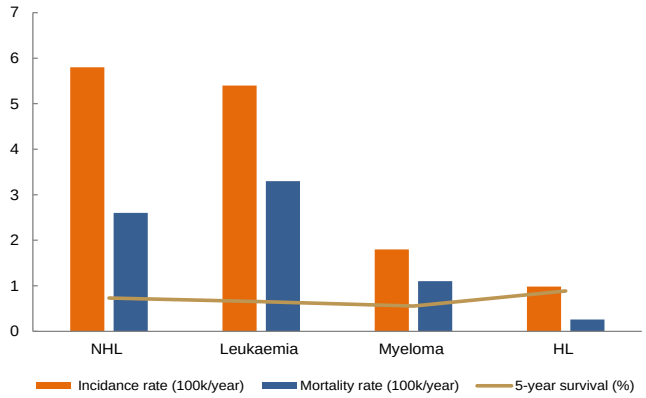
Myeloma	Incidence rate in US (per 100k)	5 yr Survival rate	1L Treatment	2L+ Treatment	New trend & clinical progress
MM	**7.1**	**57.9%**	**1. Triple therapy** **protease inhibitor+ I/O + corticosteroid)** (e.g. bortezomib, lenalidomide, dexamethsone) **2. CD38 mAb** e.g daratumumab **3. BCMA ADC** e.g Belantamab mafodotin-blmf, Blenrep	**1. auto-SCT** e.g Tki + Blinatumomab **2. BCMA CAR-T therapy** e.g. BCMA CAR-T cells, idecabtagene vicleucel, Abecma) **3. BCMA ADC** e.g, Blenrep	• BiTE (BCMA xCD3) • BiTE (GPRC5D xCD3) • BCMA CAR-T • GPRC5D CAR-T • BCMA CAR-NK • BCL-2 (venetoclax) • XPO1 (selinexor)

Sources: CMS (HK); NCCN guideline，5-year survival 2012-2018

Appendix C: Lead products and consensus sales forecast

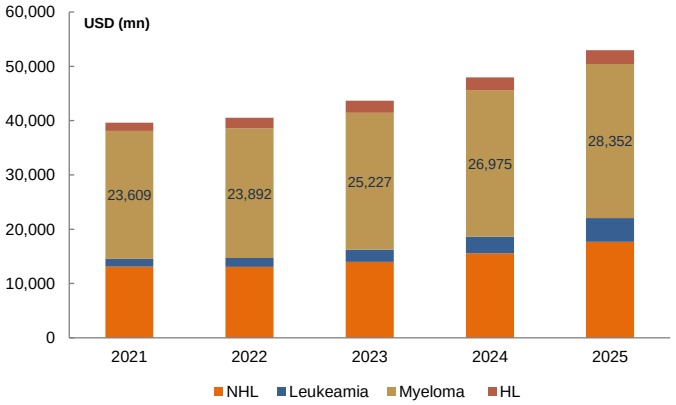
Appendix C1: haematological cancer disease burden and sales forecast

Disease burden and sales forecast for major HC types



Type of cancer	Incidence (100k/year)	Mortality rate (100k/year)	5-year survival (%)
NHL	5.8	2.6	73.20%
Leukemia	5.4	3.3	65%
Myeloma	1.8	1.1	55.60%
HL	0.98	0.26	88.30%

Sales forecast by indication

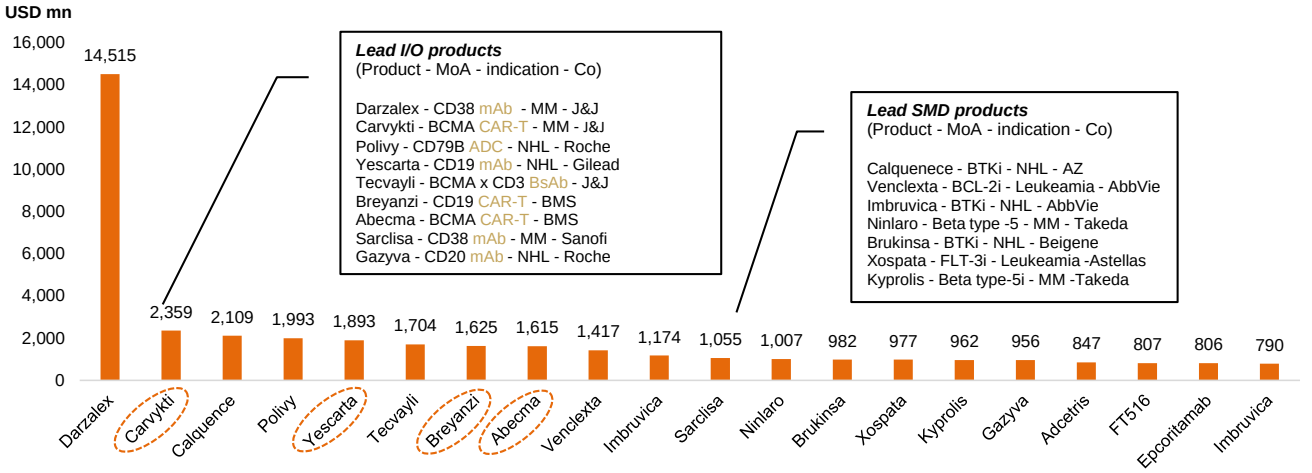


Type of cancer	2021	2022	2023	2024	2025
NHL	13,090	13,076	13,974	15,565	17,671
Leukemia	1,431	1,634	2,266	3,077	4,395
Myeloma	23,609	23,892	25,227	26,975	28,352
HL	1,506	1,925	2,200	2,361	2,562

Sources: CMS (HK), IQVIA 2020 white paper, HL, Hodgkin Lymphoma, NHL, non- Hodgkin Lymphoma

Appendix C2: haematological cancer lead products and sales forecast

Sales forecast by 2028 (USD mn)



Sources: CMS (HK), Evaluate pharma, red circle, CAR-T therapy

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Appendix C3: Lead products in haematology space

Product	Indication	Company	Generic name	Target	Modality	2021	2022	2023	2024	2025	2026	2027	2028	ASH Presentation
Darzalex	MM	Johnson & Johnson	daratumumab	CD38	mAb	6,023	7,894	9,505	10,891	12,043	13,020	13,821	14,515	Y
Carvykti	MM	Johnson & Johnson	ciltacabtagene autoleucel	BCMA	CAR-T	n.a	75	345	878	1,347	1,761	2,121	2,359	Y
Calquence	NHL	AstraZeneca	acalabrutinib	BTK	SMD	663	803	1,041	1,295	1,542	1,750	1,924	2,109	Y
Polivy	NHL	Roche	polatuzumab vedotin	CD79B	ADC	270	468	822	1,160	1,467	1,652	1,833	1,993	Y
Yescarta	NHL	Gilead Sciences	axicabtagene ciloleucel	CD19	CAR-T cell	695	1,135	1,273	1,415	1,521	1,644	1,789	1,893	Y
Tecvayli	MM	Johnson & Johnson	axicabtagene ciloleucel	BCMA x CD3	BsAb	n.a	n.a	n.a	373	523	804	1,180	1,704	Y
Breyanzi	NHL	Bristol Myers Squibb	lisocabtagene maraleucel	CD19	CAR-T cell	87	183	429	738	988	1,244	1,435	1,625	Y
Abecma	MM	Bristol Myers Squibb	idecabtagene vicleucel	BCMA	CAR-T	164	360	569	808	1,050	1,300	1,463	1,615	Y
Venclexta	AML, CLL	AbbVie	venetoclax	BCL-2	SMD	426	607	826	1,006	1,144	1,255	1,340	1,417	Y
Imbruvica	NHL	AbbVie	ibrutinib	BTK	SMD	1,060	967	1,035	1,072	1,103	1,132	1,133	1,174	Y
Sarclisa	MM	Sanofi	isatuximab	CD38	mAb	208	320	477	617	773	908	989	1,055	Y
Ninlaro	MM	Takeda	ixazomib citrate	beta type-5	SMD	813	824	881	935	998	1,044	1,019	1,007	N
Brukinsa	NHL	BeiGene	zanubrutinib	BTK	SMD	184	228	375	562	753	919	943	982	Y
Xospata	AML	Astellas Pharma	gilteritinib fumarate	FLT-3	SMD	304	372	451	538	656	769	873	977	N
Kyprolis	MM	Amgen	carfilzomib	beta type-5	SMD	1,108	1,218	1,294	1,390	1,362	1,348	1,275	962	Y
Gazyva	NHL	Roche	obinutuzumab	CD20	mAb	570	615	676	721	784	853	912	956	
Adcetris	HL	Seagen	brentuximab vedotin	TNFRSF8	ADC	514	477	533	592	632	694	772	847	Y
FT516	NHL	Fate Therapeutics	n.a	NK cell therapy	T-Cell			23	101	268	439	608	807	N
Epcoritamab	NHL	Genmab	epcoritamab	CD20	mAb			49	185	352	509	670	806	N
Imbruvica	NHL	Johnson & Johnson	ibrutinib	BTK	SMD	663	677	751	668	714	748	778	790	Y

Sources: Evaluate, CMS (HK); ASH 2022, company news; Grey, key China product highlight; Y: yes, N: no

Investment risk

Clinical failure of clinical assets; Worse than expected data readout; Regulatory delay.

Investment Ratings

Industry Rating	Definition
OVERWEIGHT	Expect sector to outperform the market over the next 12 months
NEUTRAL	Expect sector to perform in-line with the market over the next 12 months
UNDERWEIGHT	Expect sector to underperform the market over the next 12 months

Company Rating	Definition
BUY	Expect stock to generate 10%+ return over the next 12 months
HOLD	Expect stock to generate +10% to -10% over the next 12 months
SELL	Expect stock to generate loss of 10%+ over the next 12 months

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