

Dendritic cell (DC) immunotherapy in myeloid leukemia

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Disclosures of commercial support

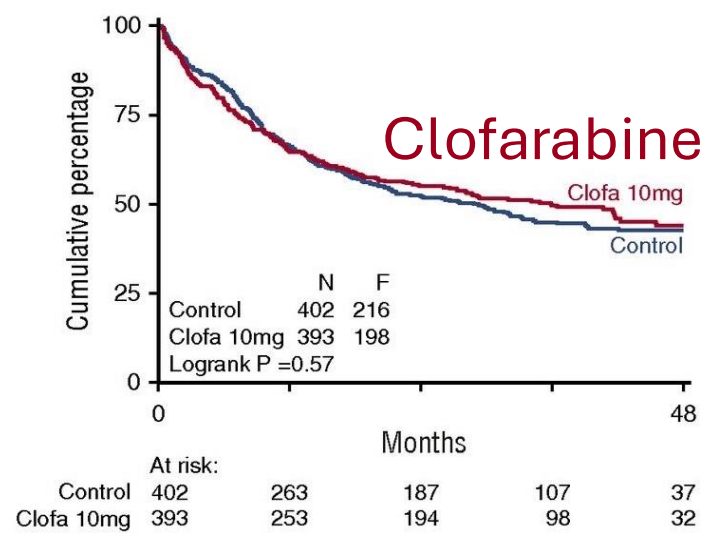
Consultancy – AOP Orphan Pharmaceuticals GmbH, Astellas Pharma, AstraZeneca, Daichii Sankyo, Delbert Pharma, Incyte, JAZZ Pharmaceuticals, Johnson & Johnson, KinSea Lead Discovery AS, Kyowa Kirin, Mendus, MSD, Novartis, Otsuka Pharma, Sanofi, Vivesto,

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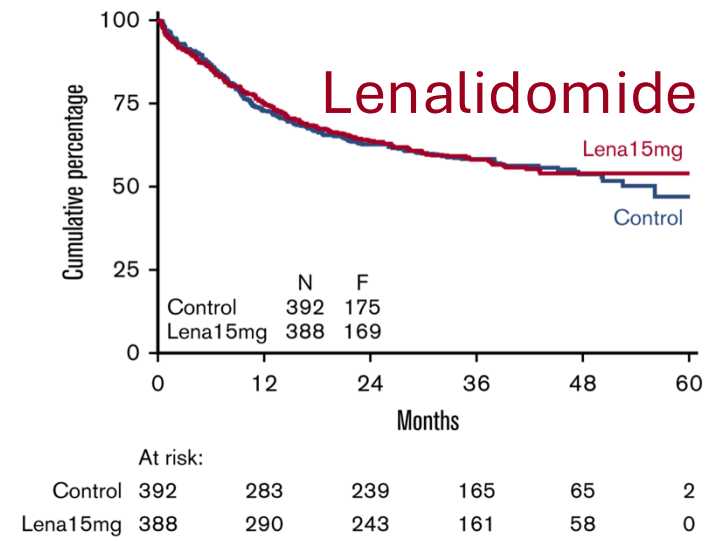
Equity Holder – Alden Cancer Therapy AS, Há Biotech AS, Kinn Therapeutics AS, Bjørgvin Therapeutic Group AS

Acute myeloid leukemia (AML) HOVON Phase III RCT: 18-65 y, intensive chemotherapy, new combinations versus standard therapy

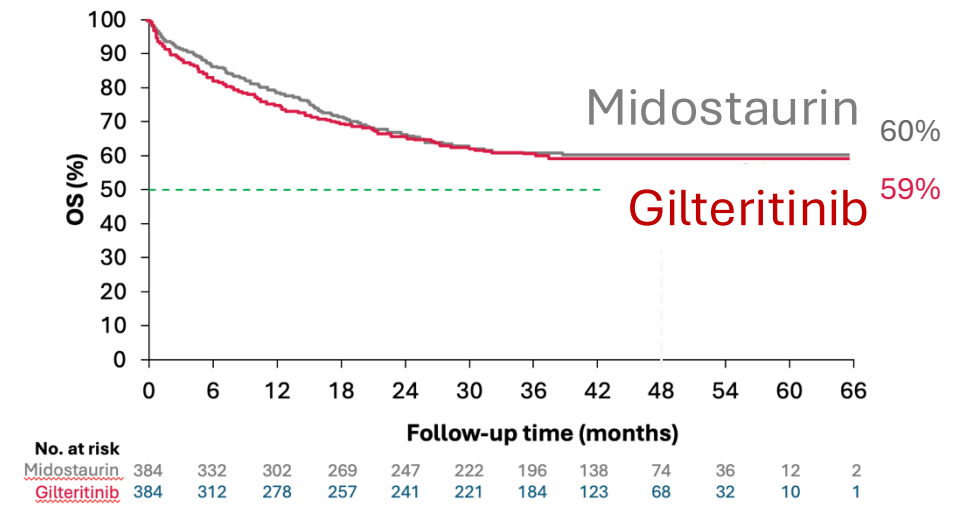
Overall survival by induction treatment



Löwenberg B, et al. Blood 2017



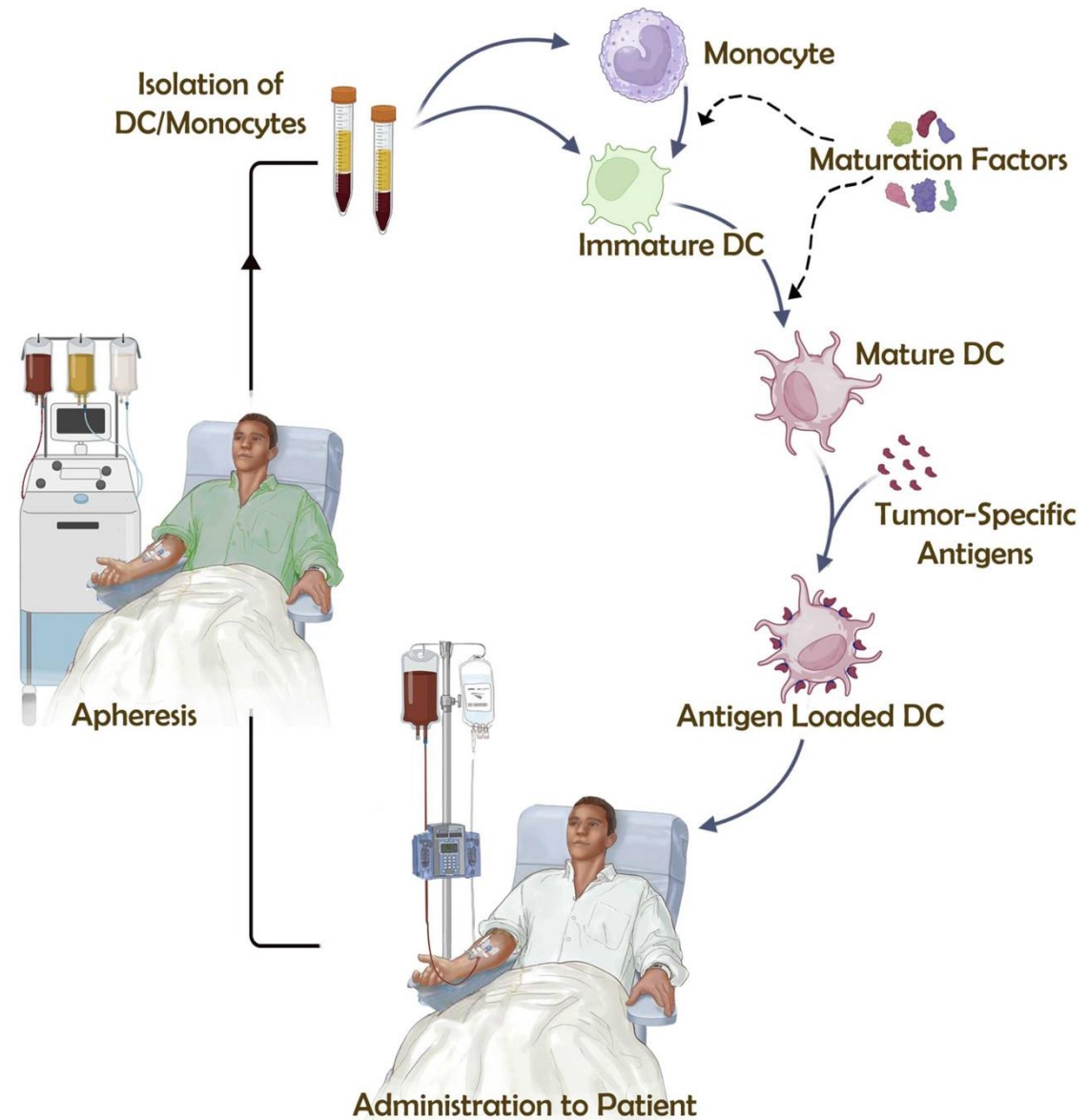
Löwenberg B, et al. Blood 2021



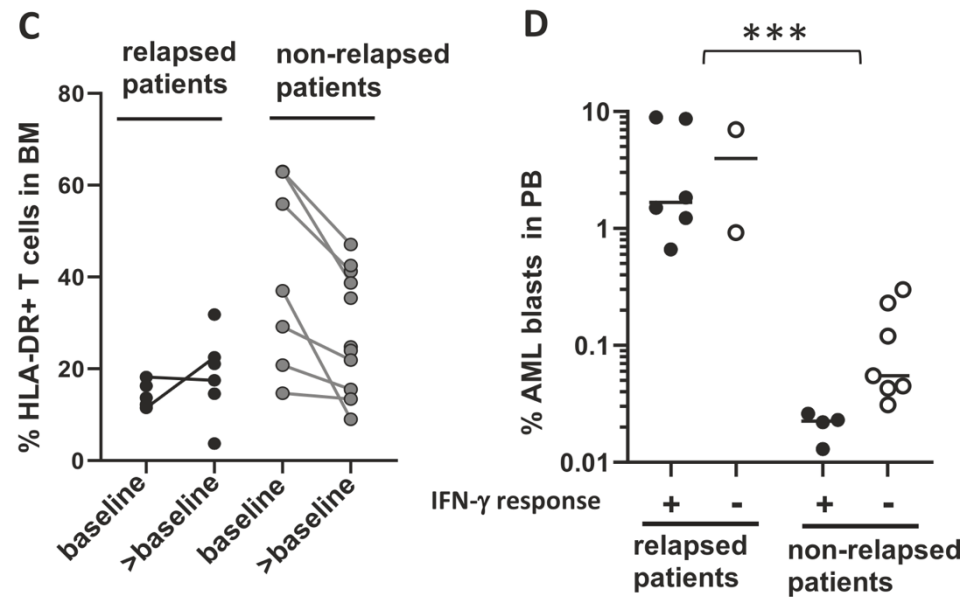
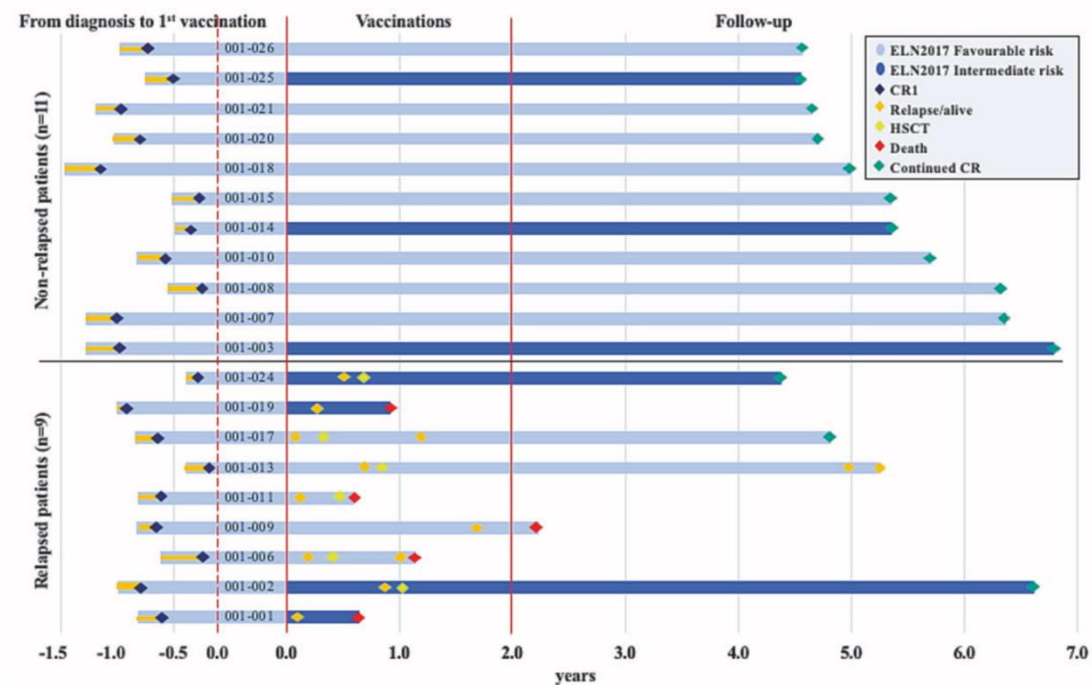
Raaijmakers M, et al. EHA 2026 EHA-7247

Unmet need for safe post-remission therapies that enable durable clinical remissions, while preserving health and quality of life

DC vaccine generation from peripheral blood monocytes obtained by leukapheresis, mDCs, loaded individually with either WT1 or PRAME ivt-RNA, were cryopreserved in multiple aliquots for intradermal injection after thawing, centrifugation and resuspension

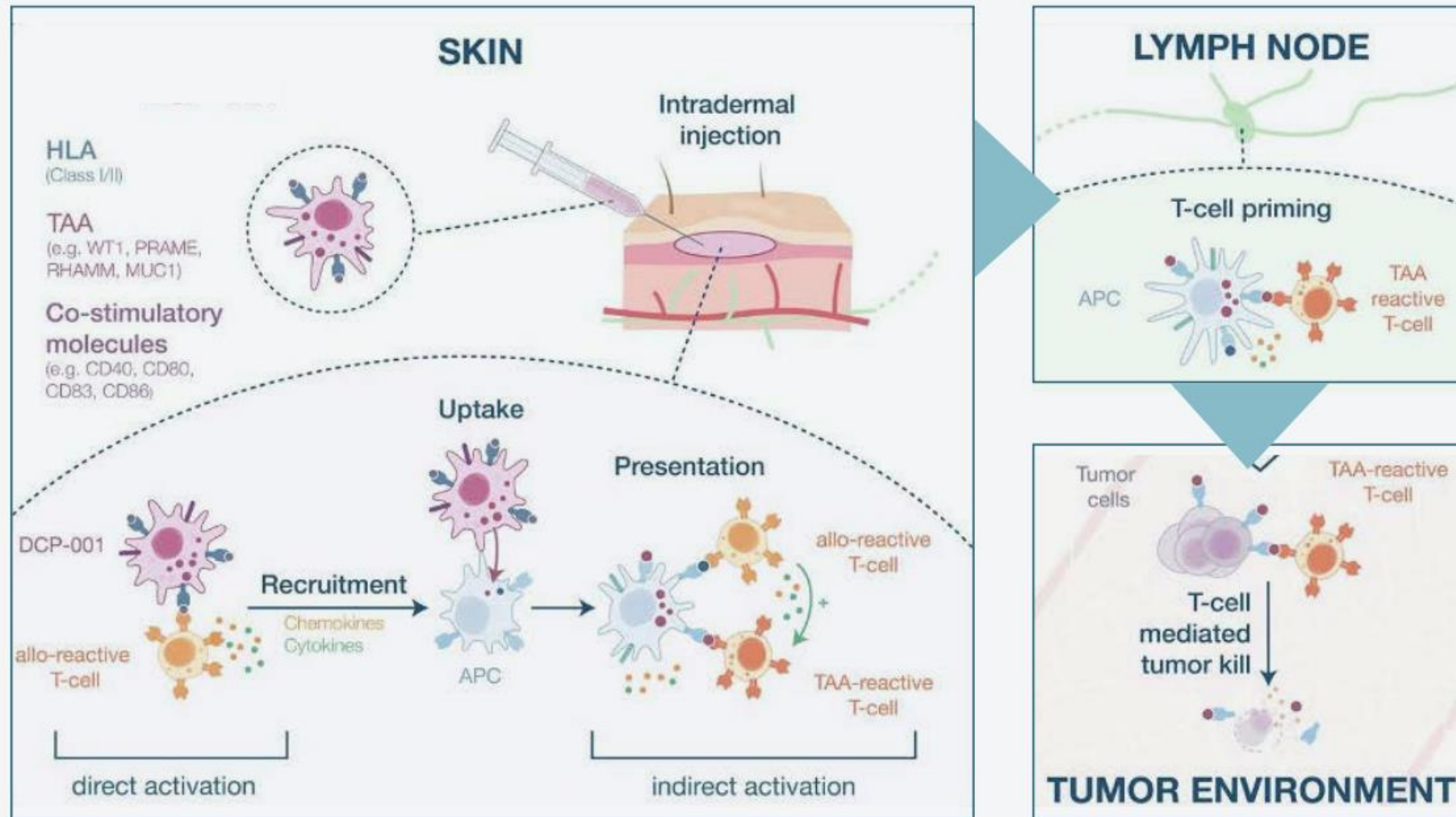


WT1 and PRAME RNA-loaded dendritic cell vaccine in de novo AML after intensive chemotherapy

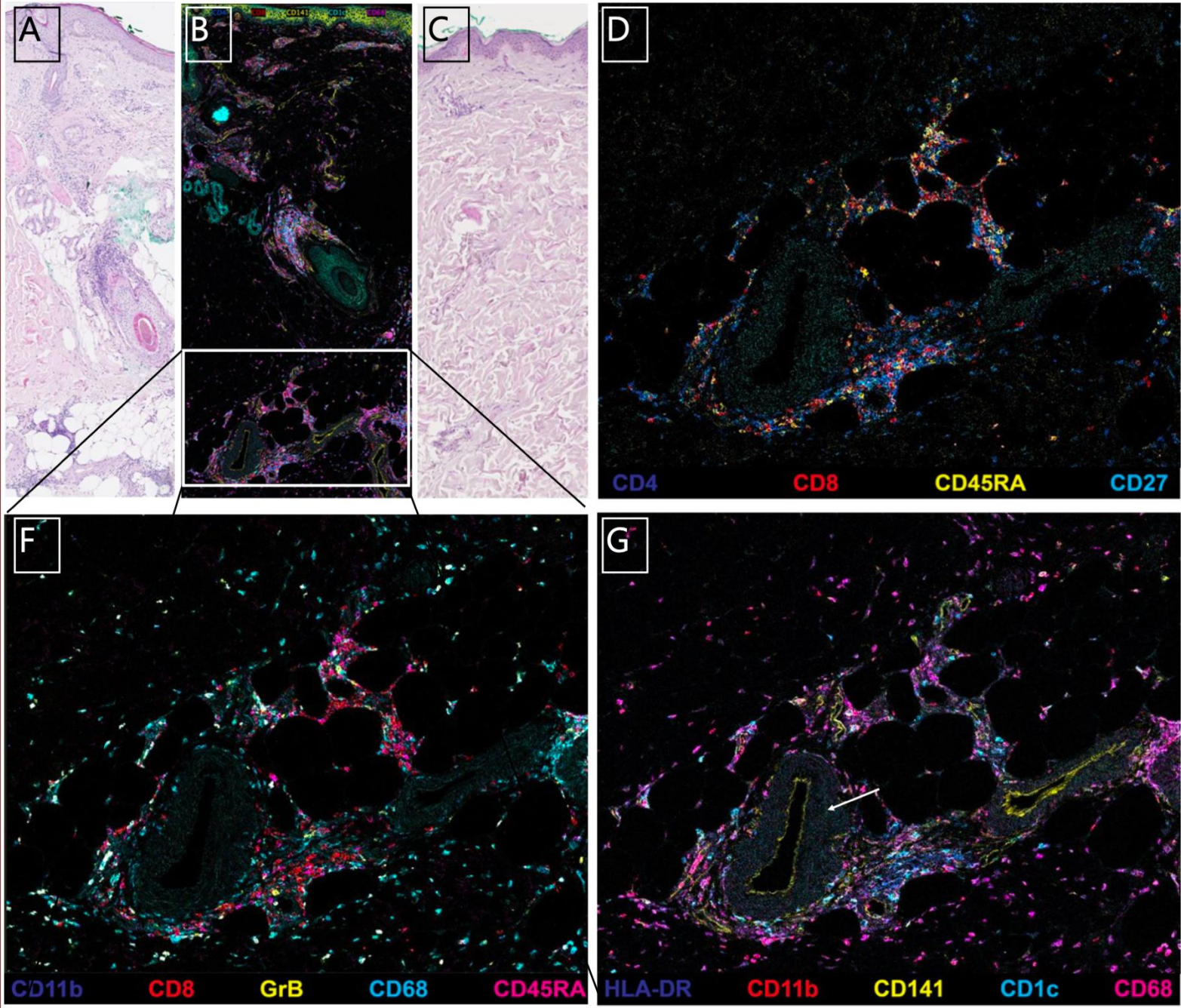
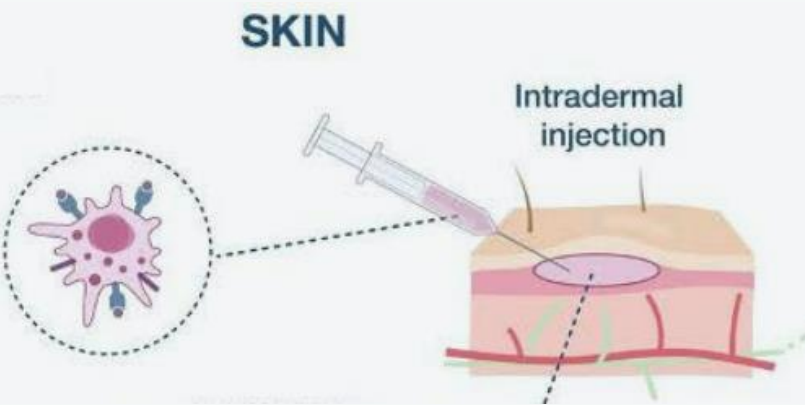


Eleven of 20 patients (55%) remained in CR, while 4 of 6 relapsing patients achieved CR2 after salvage therapy and underwent allo-HSCT. OS at 5 years was 75% (95% CI: 50–89), with 70% of patients ≥60 years of age being long-term survivors.

Vididencel immunotherapy: mechanism of action



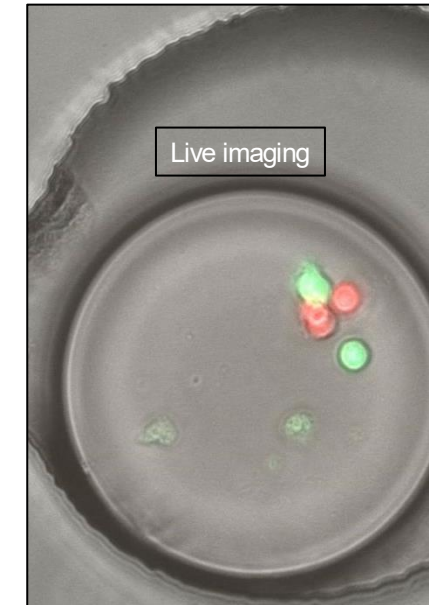
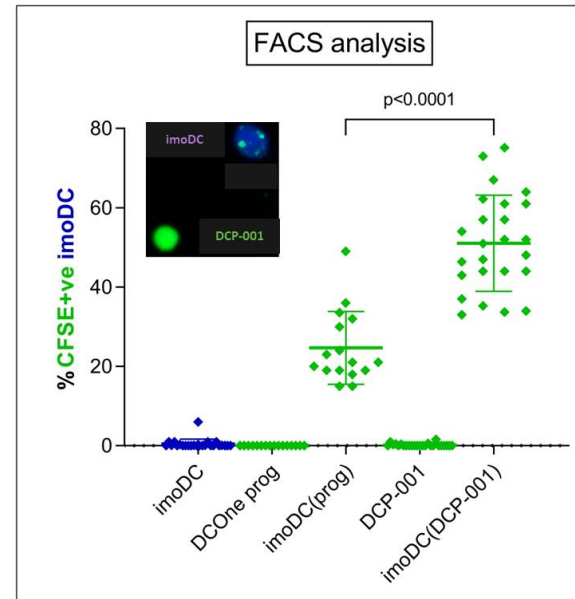
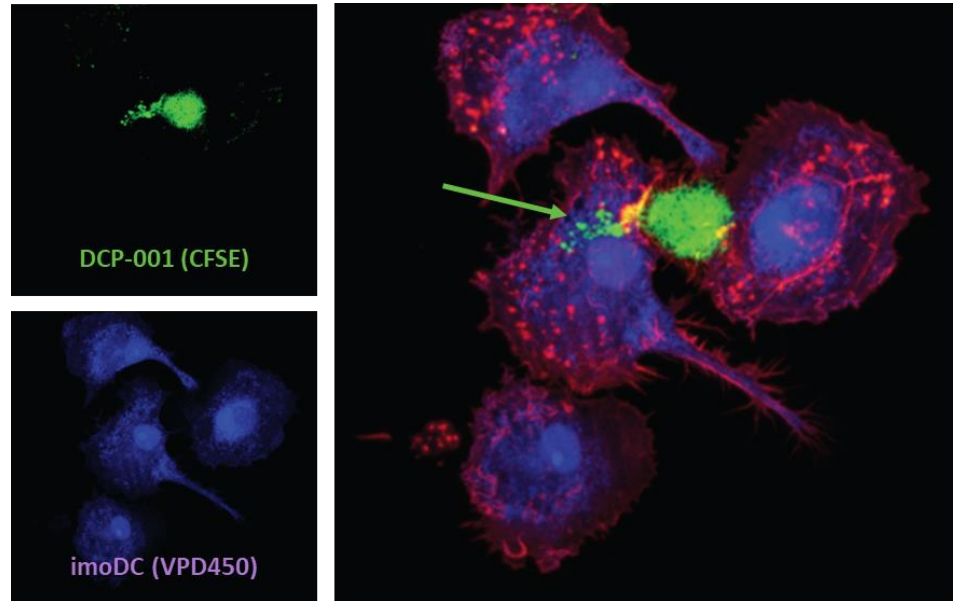
Skin biopsies 2 days
after 4th injection
vididencel



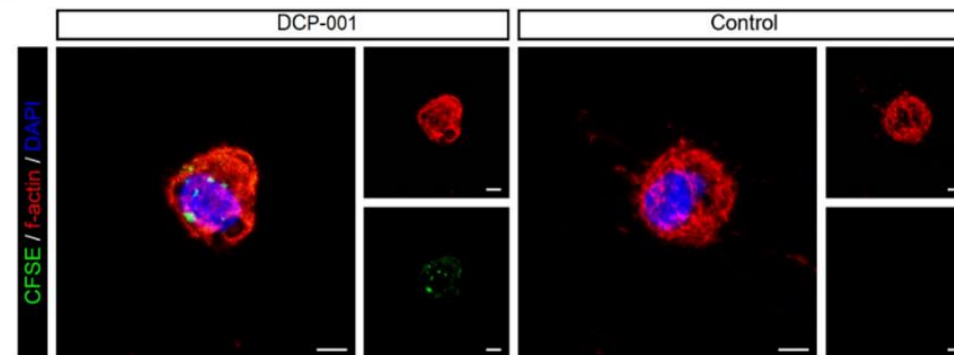
Vididencel transfers cellular content to host APCs

Direct cell-cell interactions triggering phagocytosis and activation

Vididencel (DCP-001) triggers phagocytosis by APC (imoDC) *in vitro* (below and right)*



Upon intradermal injection, vididencel (DCP-001) cellular content is phagocytosed by skin-resident APC, which become activated during the process (right)

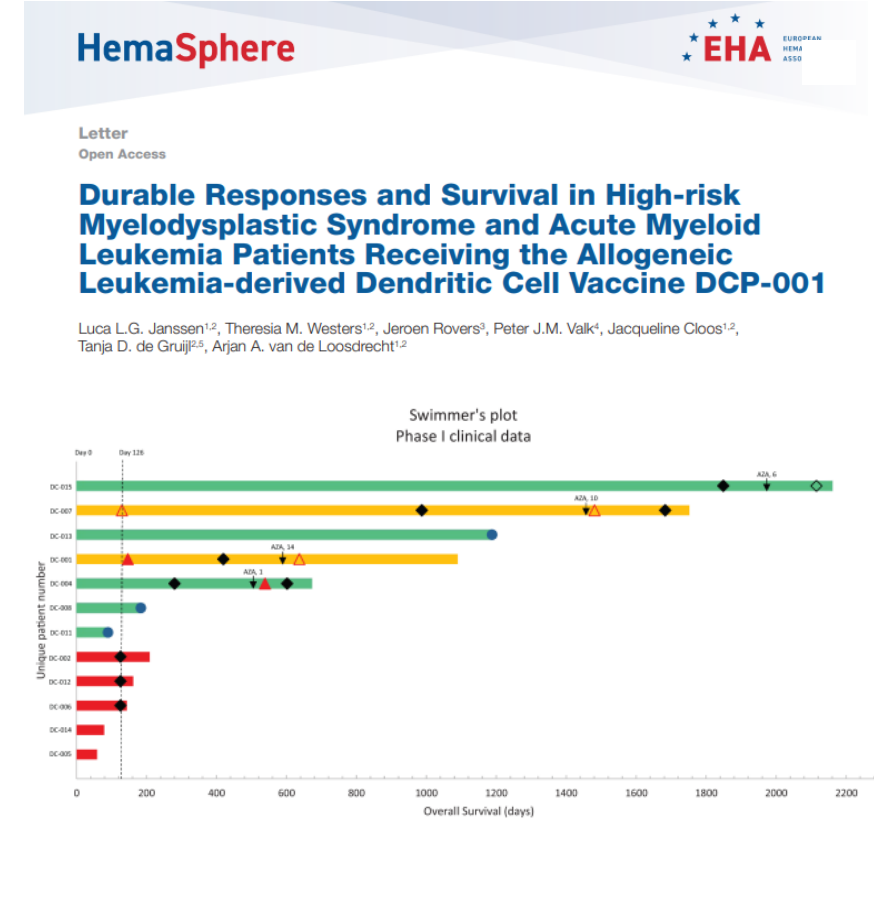


Phase 1 vididencel trial confirms safety and feasibility

Best responses in patients with low disease burden

- Clinical evidence that vididencel (Product ID: DCP-001) is safe, tolerable and feasible as an immunotherapy in AML and high-risk MDS
- Vididencel induces cellular and humoral responses against leukemic antigens
- Patients with low disease burden have the best chance to respond to vididencel treatment
- Median OS of 35.8 months in patients with <10% bone marrow blasts at study entry
- Patients with adverse cytogenetic risk profile may still respond to vididencel therapy

“....We observed no association between response and risk groups as established by the 2017 ELN, 2022 ELN, or IPSS-R criteria, diagnosis (WHO 2008, WHO 2022), dose cohort, adverse event, (only local skin reactions), cytogenetic aberrancies and mutations”



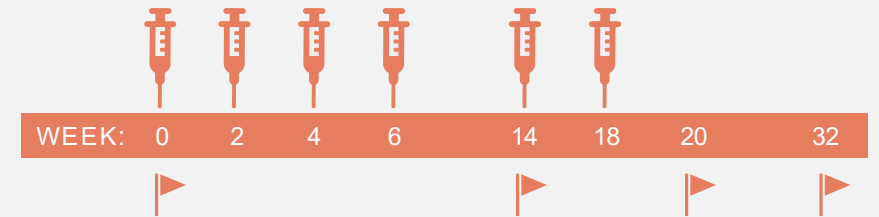
ADVANCE II Phase 2a Trial in MRD+ AML

Evaluating vididencel as post-remission therapy in a high-risk patient population

- **Design**
Open-label Phase 2 trial in 20 evaluable AML patients in first complete remission (CR1) with measurable residual disease (MRD)
- **Goal**
Evaluate vididencel as a post-remission immunotherapy to reduce relapse risk
- **Administration schedule**
6 Intradermal injections over 18 weeks
- **Sites**
Conducted across 10 European clinical centers
- **Status**
Completed, including 5 year long-term follow-up

ADVANCE II

Vididencel administration schedule



Endpoints

- Safety
- MRD assessments at baseline and Week 14, 20 and 32
- Relapse-free and overall survival
- Immune responses

Safety overview ADVANCE-II

n (%)	25x10 ⁶ cells/vacc (N=12)*	50x10 ⁶ cells/vacc (N=14)*	All (N=26)
Patients with any Adverse Event related to treatment	12 (100.0%)	14 (100.0%)	26 (100.0%)
All Adverse Event related to treatment	37	42	79
Nervous System Disorders**	0 (0.0%)	2 (14.3%)	2 (7.7%)
Headache	0 (0.0%)	1 (7.1%)	1 (3.8%)
Paraesthesia	0 (0.0%)	1 (7.1%)	1 (3.8%)
Peripheral Sensory Neuropathy	0 (0.0%)	1 (7.1%)	1 (3.8%)
Gastrointestinal Disorders**	1 (8.3%)	0 (0.0%)	1 (3.8%)
Diarrhoea	1 (8.3%)	0 (0.0%)	1 (3.8%)
Skin And Subcutaneous Tissue Disorders**	1 (8.3%)	2 (14.3%)	3 (11.5%)
Pruritus	1 (8.3%)	0 (0.0%)	1 (3.8%)
Rash Maculo-Papular	1 (8.3%)	0 (0.0%)	1 (3.8%)
Dermatitis Psoriasiform	0 (0.0%)	1 (7.1%)	1 (3.8%)
Rash Pruritic	0 (0.0%)	1 (7.1%)	1 (3.8%)
Musculoskeletal And Connective Tissue Disorders**	0 (0.0%)	2 (14.3%)	2 (7.7%)
Arthralgia	0 (0.0%)	1 (7.1%)	1 (3.8%)
Myalgia	0 (0.0%)	1 (7.1%)	1 (3.8%)
General Disorders And Administration Site Conditions**	11 (91.7%)	12 (85.7%)	23 (88.5%)
Injection Site Reaction	11 (91.7%)	12 (85.7%)	23 (88.5%)
Fatigue	0 (0.0%)	2 (14.3%)	2 (7.7%)
Severity (any grade)	12 (100%)	14 (100%)	26 (100%)
Mild (Grade 1)	11 (91.7%)	14 (100%)	25 (96.2%)
Moderate (Grade 2)	3 (25.0%)	5 (35.7%)	8 (30.8%)
Severe (Grade 3)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Life Threatening (Grade 4)	0 (0.0%)	0 (0.0%)	0 (0.0%)

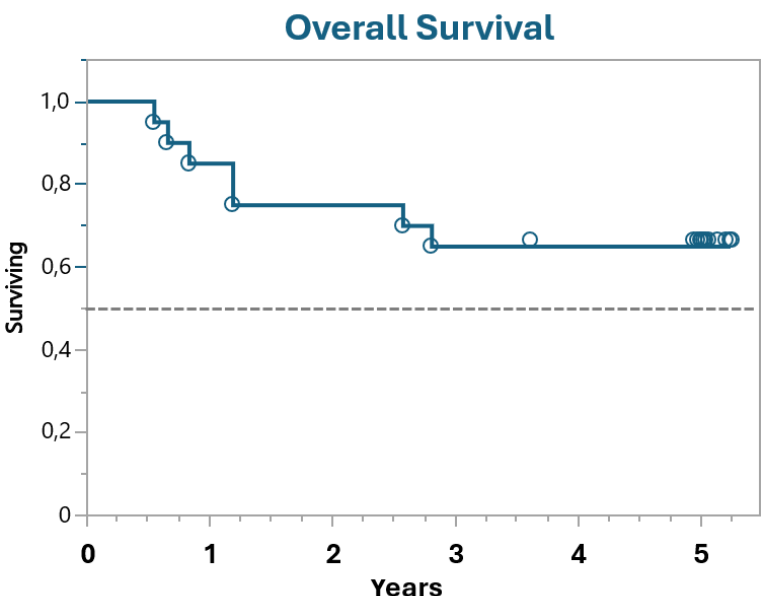
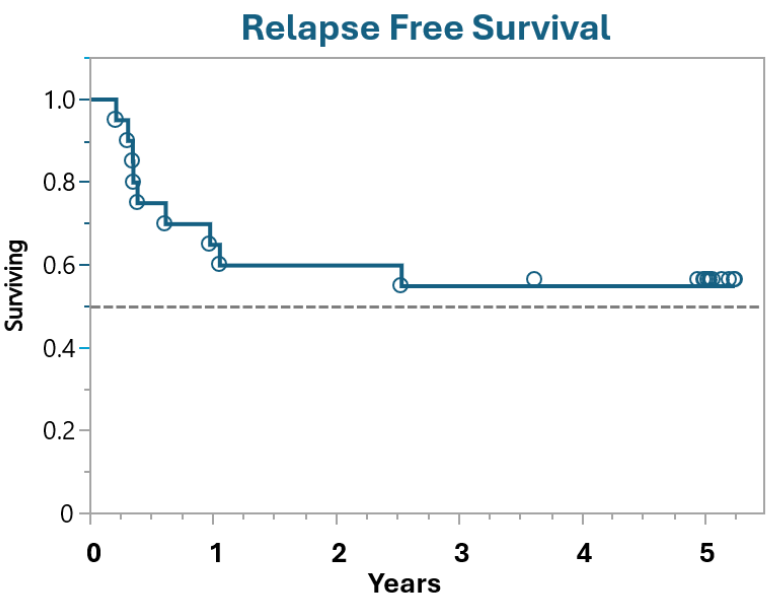
* Number of patients that received at least 1 injection of vididencel

** Patients with at least 1 Adverse Event related to treatment

Adverse Event related to treatment is when the relationship with the study treatment is possibly related, probably related or definitely related. Note: A subject could have more than one adverse event.

ADVANCE II Proof-of-Concept Data

Durable clinical remissions associated with vididencel treatment



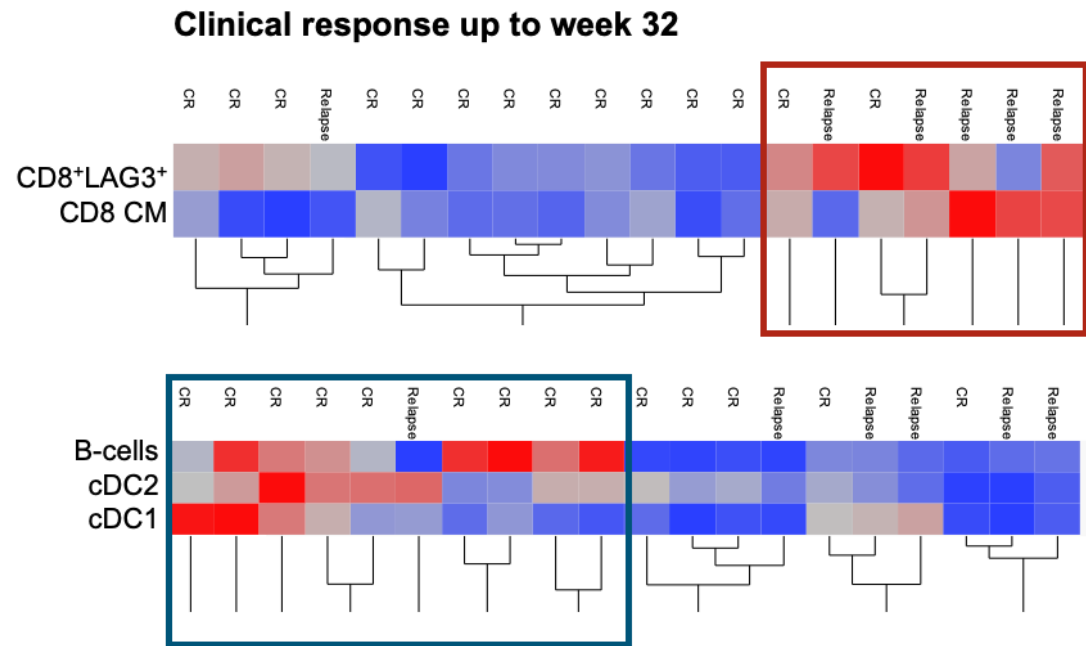
Survival parameters and range		
	RFS	OS
1 year	77% (56-88%)	88%(69%-96%)
3 year	61% (39-78%)	74% (52%-87%)
5-year estimate	52% (28-72%)	63% (38%-81%)

- Majority (**12/20**) of patients alive (and 1 lost during follow-up at 43 months) at 60-months median follow-up
- **Estimated 5-year OS: 63%** (vs < 30 % in 55 y in remission after intensive chemotherapy not HSCT candidates)*
- **Mild product-related AEs** limited to local injection reactions
- No association observed between **tumor genetics** and OS

*Source: Wei *et al.*, Am J Hematol. (2023); 98:E84–E87

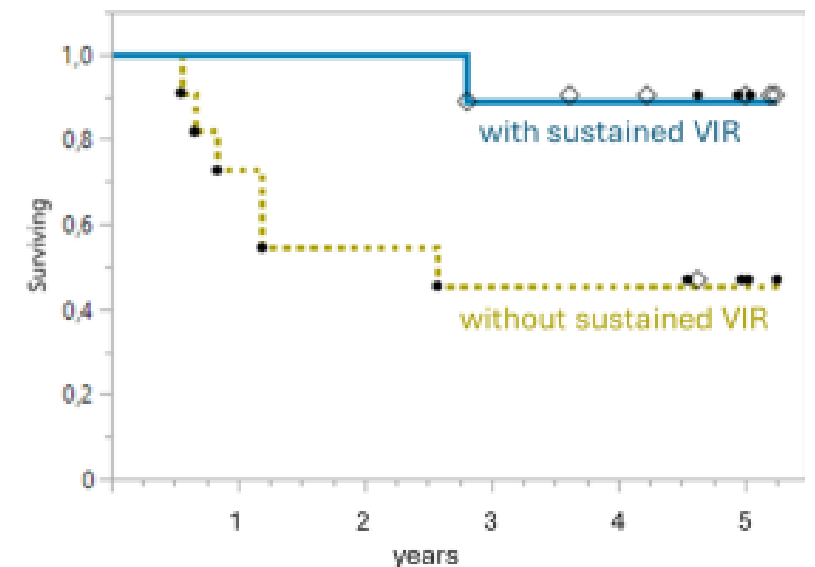
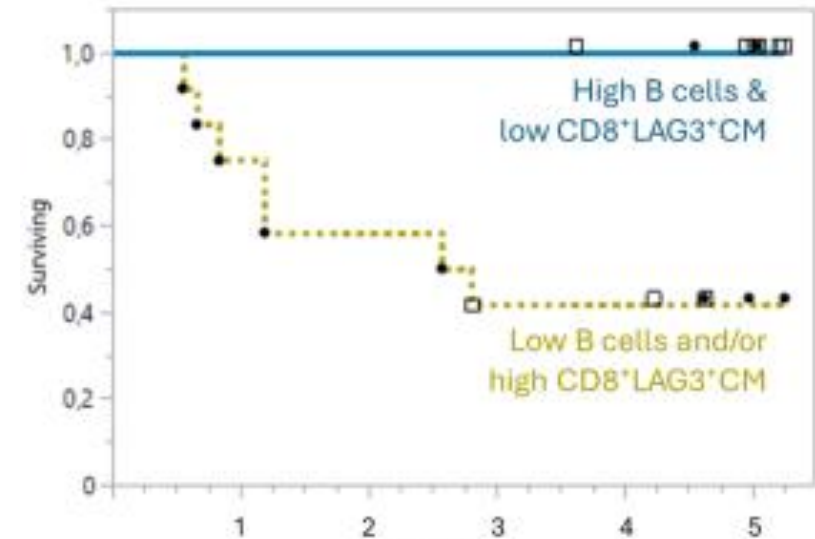
ADVANCE II Proof-of-Concept data

Immunological parameters and antigen-specific T cell responses track with survival



Heat map shows clustering of LAG3⁺/central memory CD8⁺ T cells and low levels of B cells and dendritic cells (cDC1/cDC2) to be associated with relapse

 Highest frequency
 Lowest frequency



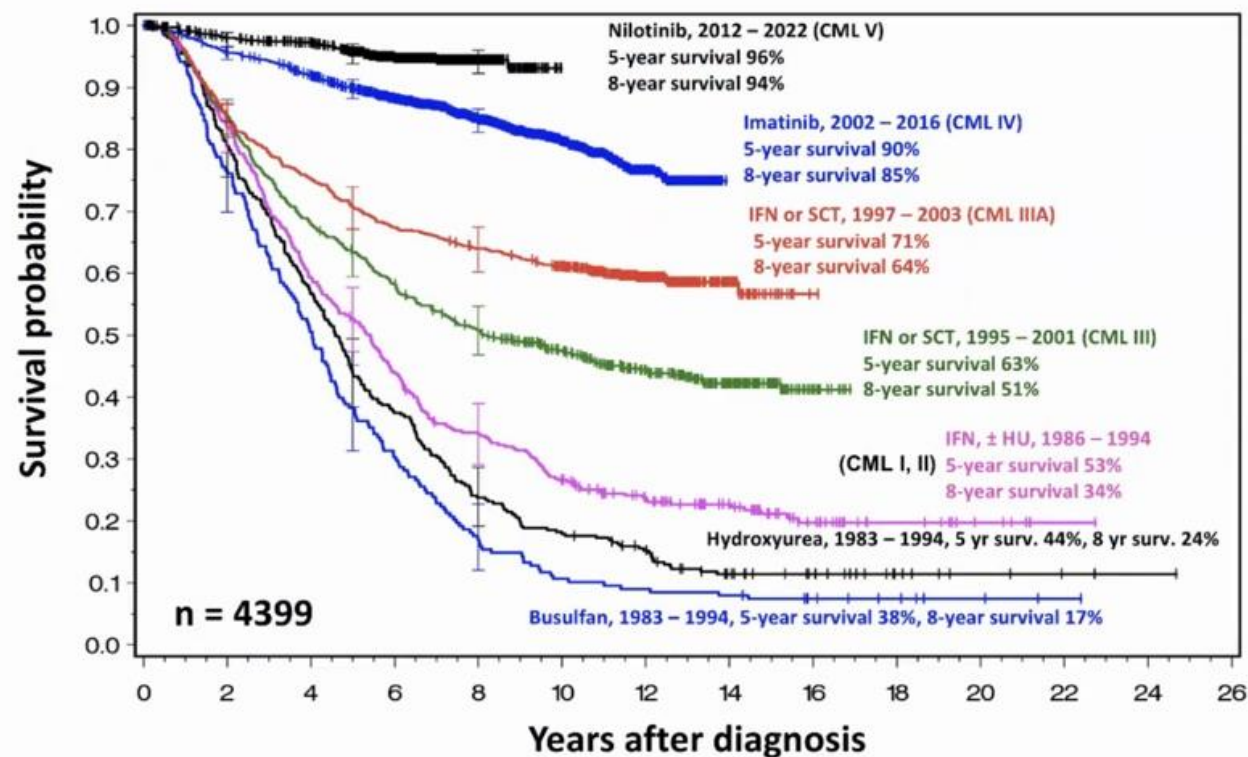
TIME

THERE IS NEW AMMUNITION
IN THE WAR AGAINST
CANCER.
THESE ARE THE BULLETS.

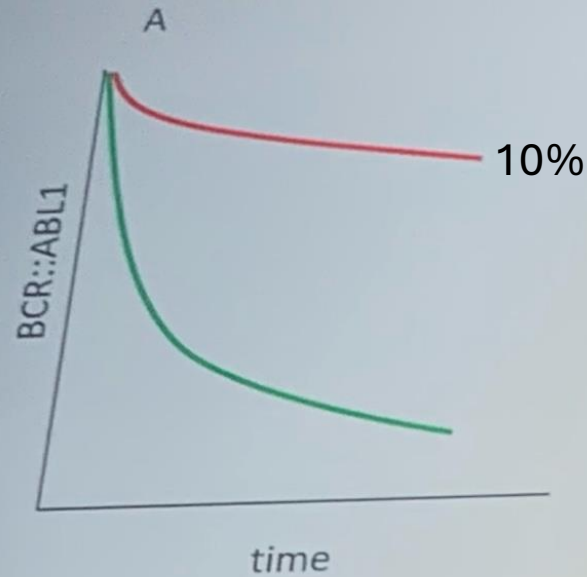
Revolutionary new pills like **GLEEVEC** combat cancer by targeting only the diseased cells. Is this the breakthrough we've been waiting for?



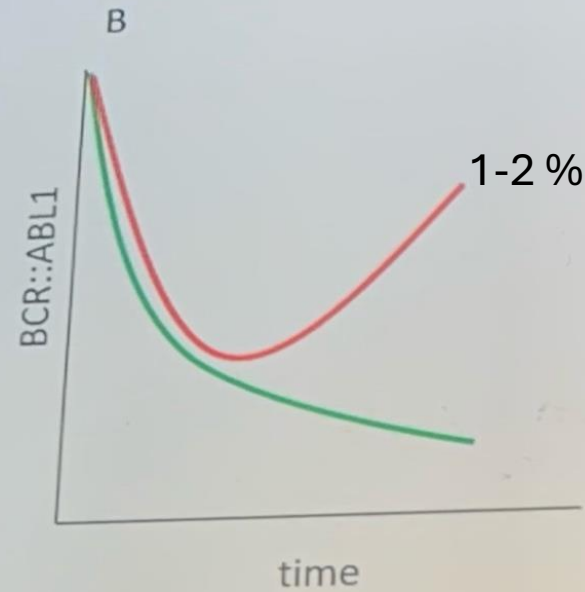
Survival with CML over time The German CML-Study Group experience



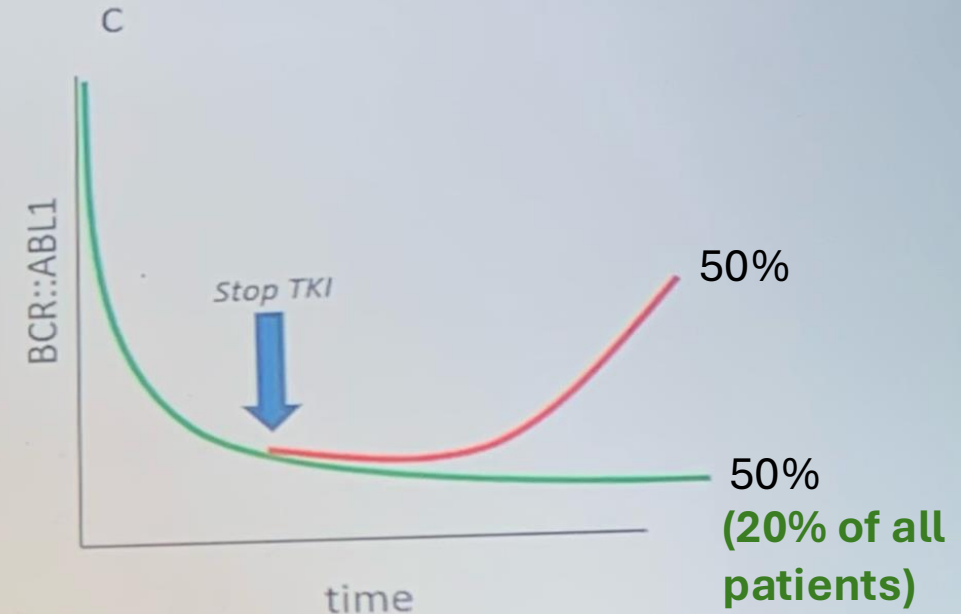
Three big questions in CML treatment



Who responds to therapy?



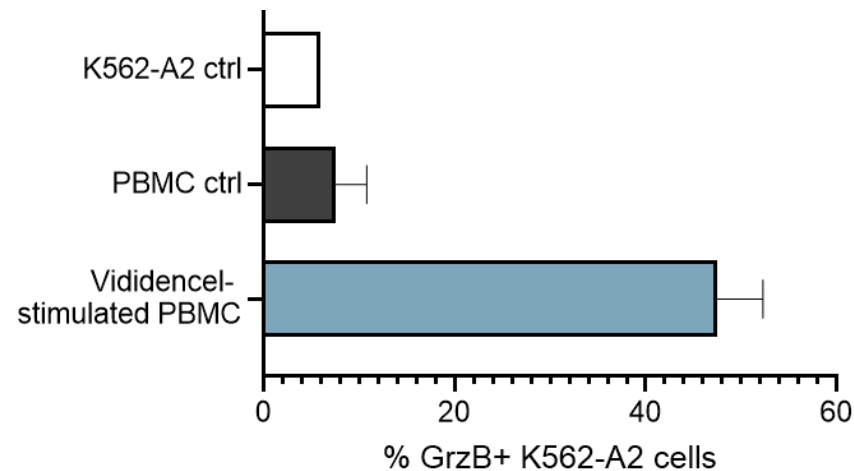
Who relapses on therapy?



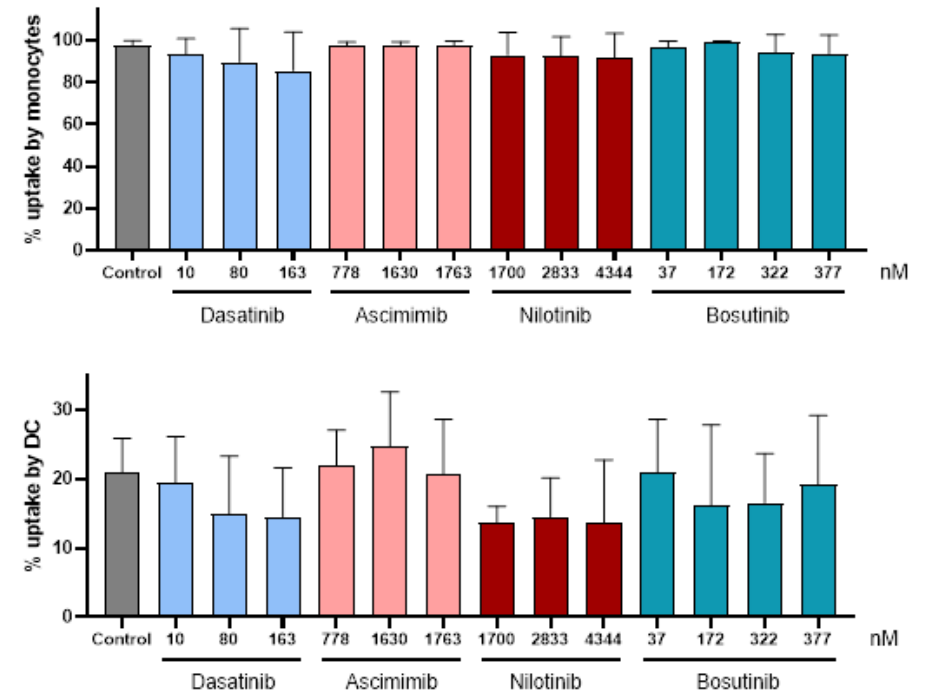
Who can discontinue therapy?

In Vitro interactions between TKIs and Leukemic-Derived Dendritic Cells As Potential Combination Therapy for Chronic Myeloid Leukemia

Vididencel-induced CTLs show cytotoxic potential against CML tumor cell line



Uptake of vididencel by monocytes or DCs is not significantly impacted after pre-exposure and in the presence of TKIs



... indicate that vididencel is a potential effective treatment for CML

VITAL-CML

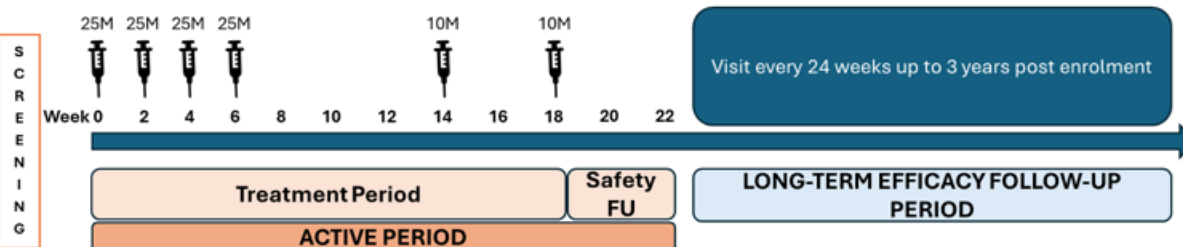
Phase 1 trial in CP-CML patients with suboptimal molecular response

Trial Design: Open-label, single center (Bergen, Norway), single-arm Phase 1 trial; Stage 1 assesses safety, tolerability and preliminary efficacy; Stage 2 assesses safety, tolerability and efficacy

Key Eligibility:

- Adults (≥ 18 years)
- CML in chronic phase; achieved MRD following treatment with an approved ABL TKI ≥ 24 months
- BCR::ABL1 transcripts $< \text{MMR } 4.0$ and stable over 6 months
- ECOG 0–1

Trial Overview



4 videncel doses of 25×10^6 cells and 2 boosters of 10×10^6 cells ; TKIs continued throughout study

Primary Objective:

- Safety and Tolerability

Secondary Objective:

- Efficacy measured as a reduction of $\geq 1 \log_{10}$ in BCR::ABL1 (IS%) levels at 3, 6, 12, 18, 24, 36 & 48 months;

Exploratory Correlatives:

- Videncel-induced immunological responses

Number of patients:

- 24 patients (interim safety & tolerability analysis after 8 patients)

Key Milestones:

- Prescreening: Dec 2025/Jan 2026 (n = 14)
- Accrual: March/Apr 2026 to Dec 2026 (n = 24)
- First Readout – Sept/Oct 2026 (n=8) : Safety/tolerability/EMR
- Second Readout– Mar/Apr 2027 (n=12); +6m & 12m BCR::ABL1
- Third Readout – Mar/Apr 2028 (n=24); +18m & 24m BCR::ABL1
- Fourth readout – Mar/Apr 2029 (n=24); +36m BCR::ABL1
- Final results – Mar/Apr 2030; +48m BCR::ABL1

Summary Vididencel Safety

- The most common adverse events observed in the ADVANCE II trial were injection site reactions (89% of subjects)
- These injection site reactions are likely caused by local immune responses, in line with the mechanism of action
- No product-related AEs above grade 2 were reported
- Overall, the feasibility and safety of vididencel have been established in AML

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