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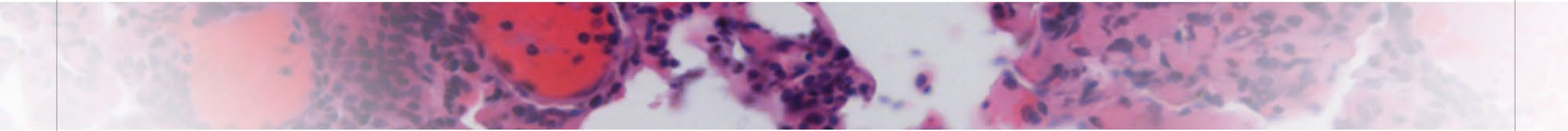


γ9δ2 T-cell Activation with ICT01 and Azacitidine-Venetoclax Induces High Rates of Remission and Overall Survival in Patients with Newly Diagnosed Acute Myeloid Leukemia

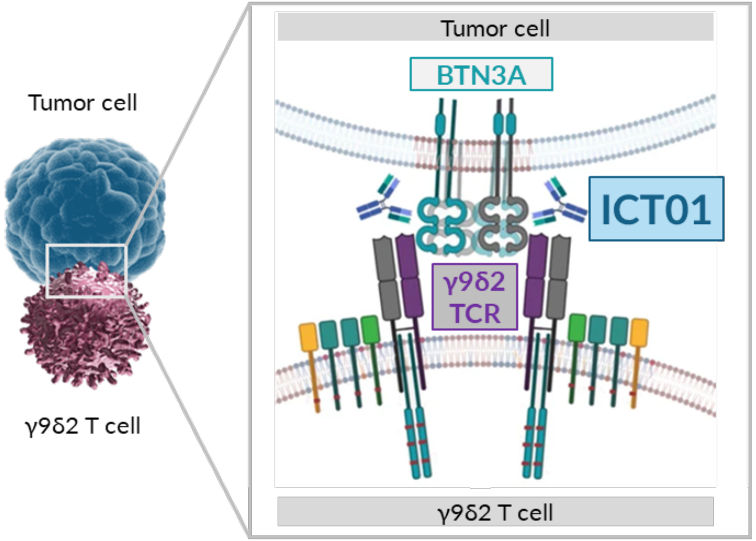
Results from the Phase 1/2 study EVICTION

Sylvain GARCIAZ, Pierre-Yves DUMAS, Pierre PETERLIN, Daniel MORILLO GILES, Jose Miguel TORREGROSA DIAZ, Matthew ULRICKSON, Agustin PENEDO, Paul KOLLER, Aude DE GASSART, Emmanuel VALENTIN, Maelle MAIRESSE, George SAAD, Patrick BRUNE, Katrien LEMMENS, Noemi ANGELOSANTO, Norbert VEY, Daniel OLIVE, Stephan BRAUN, Naval DAVER, Abhishek MAITI

Study EVICTION (NCT04243499) is sponsored by ImCheck Therapeutics SAS, Marseille, France

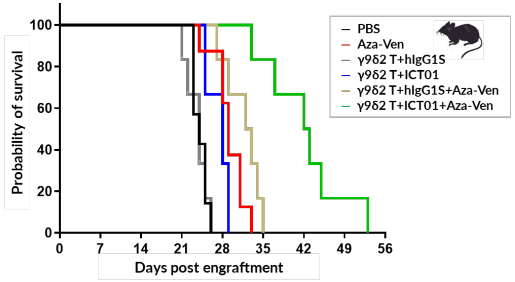
Background

- **40% of unfit AML patients treated with VEN-AZA are refractory and/or relapse within first year**[1]
- Activated γ9δ2 T cells drive graft-versus-leukemia (GVL) efficacy[2]
- **ICT01 — anti-BTN3A antibody** selectively activates γ9δ2 T cells and shows anti-leukemic activity *in vitro/vivo*[3,4]
- **ICT01** switches BTN3A on tumor cell to 'active' conformation ? Direct engagement with γ9δ2 TCR ? γ9δ2 T-cell activation ? IFNγ secretion with immunological cascade activation



- **In the phase 1 study γ9δ2 : ICT01 monotherapy** was safe at 0.7–200 mg Q3W and provided early signs of efficacy in R/R AML patients[4]

- **γ9δ2 T cells** are reliably activated in the presence of **Ven-Aza**
- **ICT01 plus Ven-Aza** showed synergistic anti-leukemic activity *in vivo* **in MOLM14 Cell treated with Ven-Aza plus Adoptive γ9δ2 T-cell Transfer**



References: [1]Diamantidis et al. Front Oncol. 2025;15:15779082 | [2]Godder et al. Bone Marrow Transplant. 2007;39(12):751-7 | [3]De Gassart et al. Sci Transl Med. 2021;13:eabj0835 | [4]Garciaz et al. Ann Oncol. 2023;34:S543 | [6]Wieduwild et al. Blood 2023;142(suppl 1):1552.

Dose-optimization Study Design for ICT01-Aza-Ven

Dose-finding Phase (N=35)

Dose-expansion Phase

EVICTION, Cohort F

Patients with ND AML
≥75 years
or
unfit for intensive CTX
(NCT04243499)

R

ICT01^high^-Ven-Aza *Q4W* (N=16)

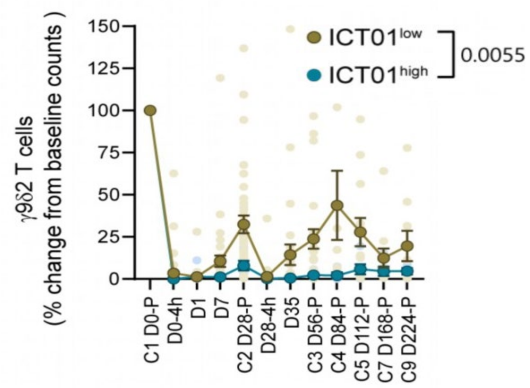
75 mg ICT01 – sustained γ9δ2T-cell activation

ICT01^low^-Ven-Aza *Q4W* (N=19)

10 mg ICT01 – transient γ9δ2T-cell activation

RP2D

ICT01^low^-Ven-Aza
(N=22)



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RP2D

ICT01$^{\text{low}}$-Ven-Aza
(N=22)

Primary Endpoint

- **Complete response (CR) rate** per ELN 2022 criteria

Key Secondary Endpoints

- Safety (incidence of TEAE as per CTCAE v5)
- CRc rate = proportion of patients with CR or CR with partial (CRh) / incomplete (CRi) hematological recovery
- Duration of response (DoR), overall survival (OS)

Inclusion criteria

- AML (WHO criteria), *TP53^{mt}* MDS/AML (ICC 2022)
- Newly diagnosed, aged ≥75 years, or 18–74 years with comorbidities & ineligible for intensive chemotherapy

Exclusion criteria

- t(15;17), t(8;21), inv(16), or t(16;16)
- Prior MPN, PV, CML or AML with t BCR-ABL1
- Prior Ven exposure

Patient Demographics & Disease Characteristics

Variables	ICT01^{low} Aza-Ven (N=41)	ICT01^{high} Aza-Ven (N=16)	Pooled (N=57)
Age [median (range)]	76 (51–87)	75 (64–84)	76 (51–87)
≥ 75 years [n(%)]	21 (51)	9 (56)	30 (53)
Male [n(%)]	25 (61)	7 (44)	32 (56)
ECOG ≥ 2 [n(%)]	12 (29)	6 (38)	18 (32)
Secondary AML[1] [n(%)]	14 (34)	5 (31)	19 (32)
Therapy-related	8 (20)	3 (19)	11 (19)
Prior MDS	6 (15)	2 (13)	8 (14)
Bone marrow blasts [median% (range)]	40 (7–98)	35 (9–82)	40 (7–98)

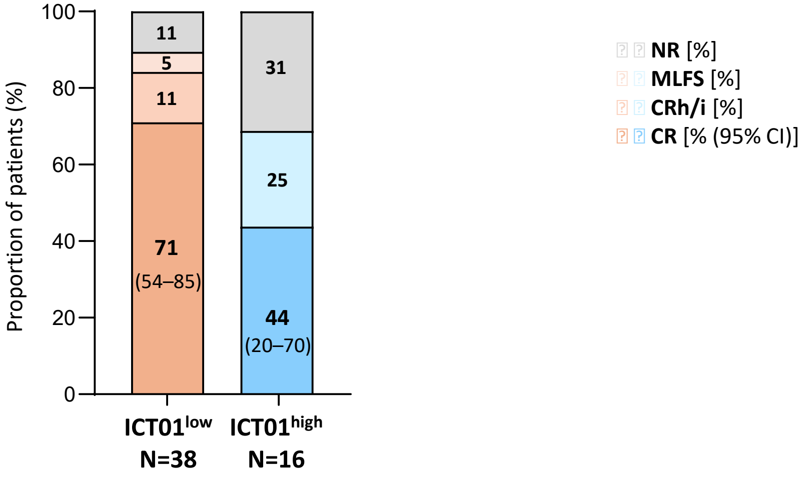
Variables	ICT01^{low} Aza-Ven (N=41)	ICT01^{high} Aza-Ven (N=16)	Pooled (N=57)
Classifying Mutations* [n(%)]			
NPM1	2 (5)	2 (13)	4 (7)
IDH1/2	9 (22)	—	9 (16)
FLT3-ITD	2 (5)	—	2 (3)
NRAS	1 (2)	1 (6)	2 (3)
KRAS	1 (2)	2 (13)	3 (5)
TP53	12 (29)	9 (56)	21 (37)
Refined ELN 2024[2] [n(%)]			
Favorable	14 (34)	2 (12)	16 (28)
Intermediate	14 (34)	3 (19)	17 (30)
Adverse	13 (32)	11 (69)	24 (42)

*<25% missing data for classifying mutations.

References: [1]Arber D.A. et al Blood 2016;127(20):2391–2405 | [2]Lachowiez et al. Blood 2024;144(26):2788–92

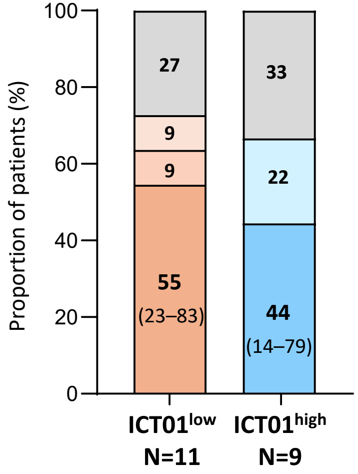
Clinical Efficacy of Ven-Aza with ICT01^{low} vs. ICT01^{high}

Best Response by Dose Cohort



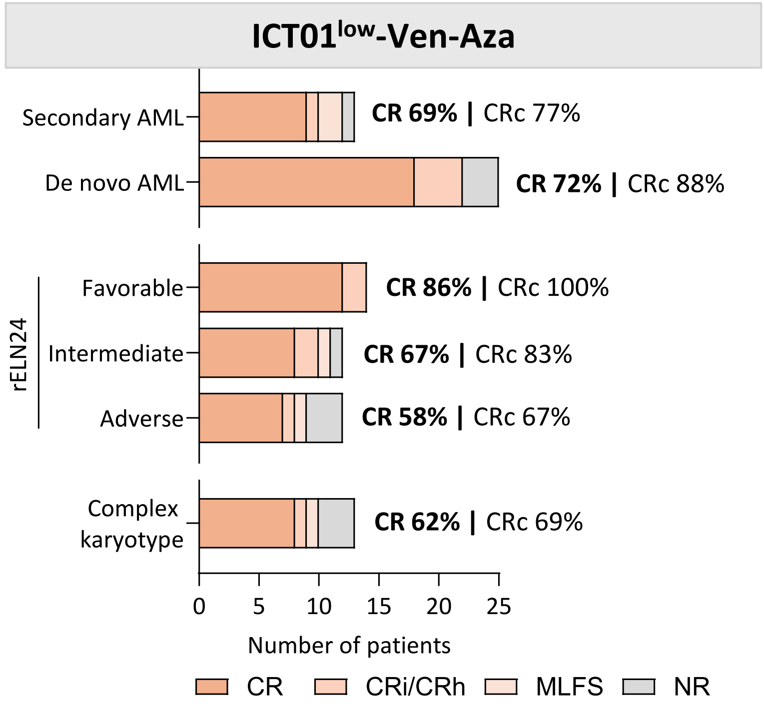
71% CR rate and 84% CRc rate

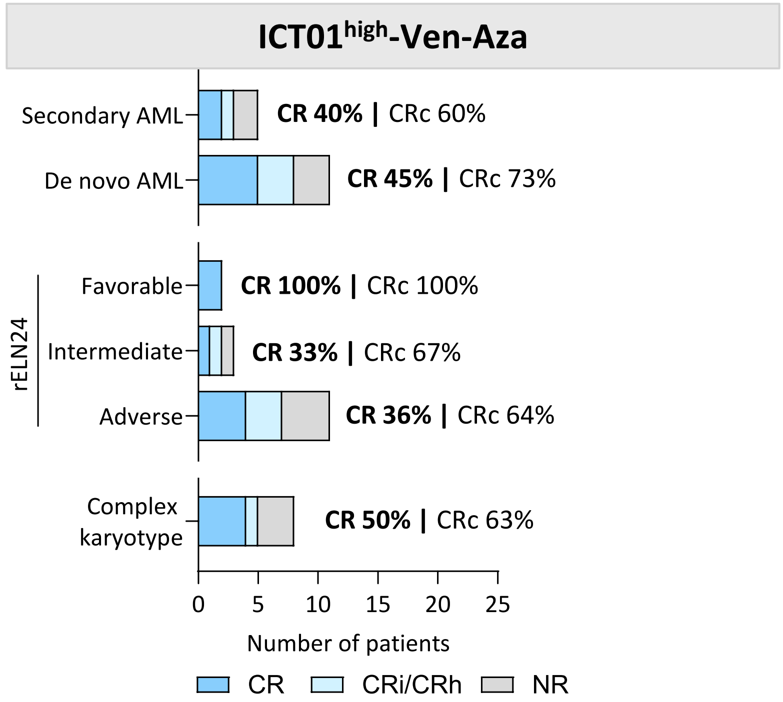
***TP53*^{mt} – Best Response by Dose Cohort**



55% CR rate and 73% CRc rate

Responses to ICT01^{low} vs ICT01^{high} by Molecular Subtypes



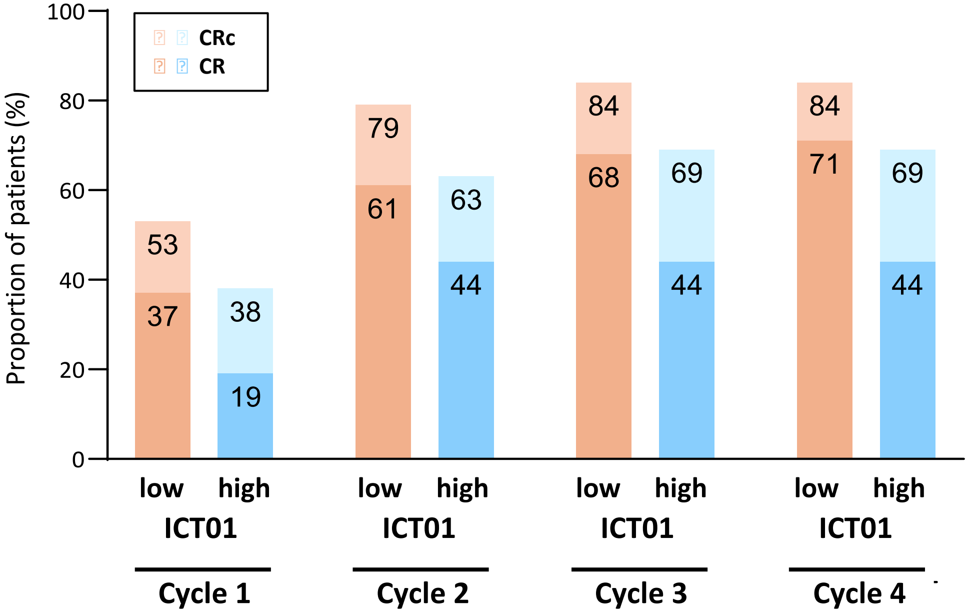


Higher response rates (CR/CRc) for patients treated with ICT01^{low} vs ICT01^{high}

Abbreviation: **rELN24**, refined ELN 2024 risk classification (Lachowiez et al. Blood. 2024:144(26):2788-2792).

Kinetics of Response and MRD analysis

CR/CRc Rates (%) by Cycle — EE population
($ICT01^{low}$ N=38; $ICT01^{high}$ N=16)



Median (range) — 4 cycles (1–24)

Days between cycles [median (IQR)]
- C1D1 to C2D1: 31d (28-37)
- C2D1 to C3D1: 31d (28-47)
- C3D1 to C4D1: 29d (28-42)
- C4D1 to C5D1: 28d (28-42)

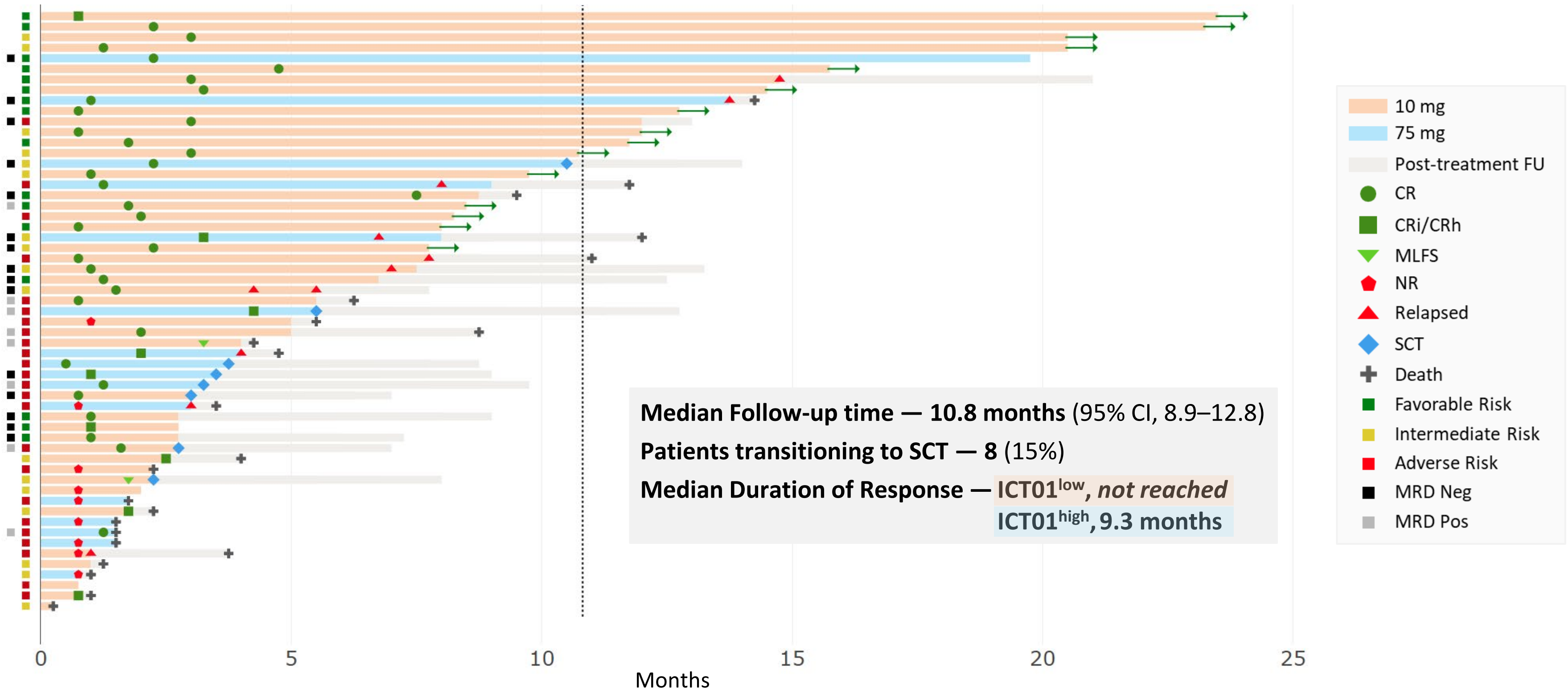
MRD Testing
(subgroup analysis)

Local MRD testing (MFC or NGS) in responders (N=23)

⇨ **CRc_{MRD-} rate**
- ⇨ **67%** (N=15) for **$ICT01^{low}$**
- ⇨ **63%** (N=8) for **$ICT01^{high}$**

<u>**Abbreviations:**</u> **EE**, efficacy-evaluable population is defined by patients having received at least 1 full cycle of ICT01-Aza-Ven treatment with disease assessments (incl. BM aspirate).

Duration of Response/Treatment with ICT01-Ven-Aza



Median Follow-up time — 10.8 months (95% CI, 8.9–12.8)

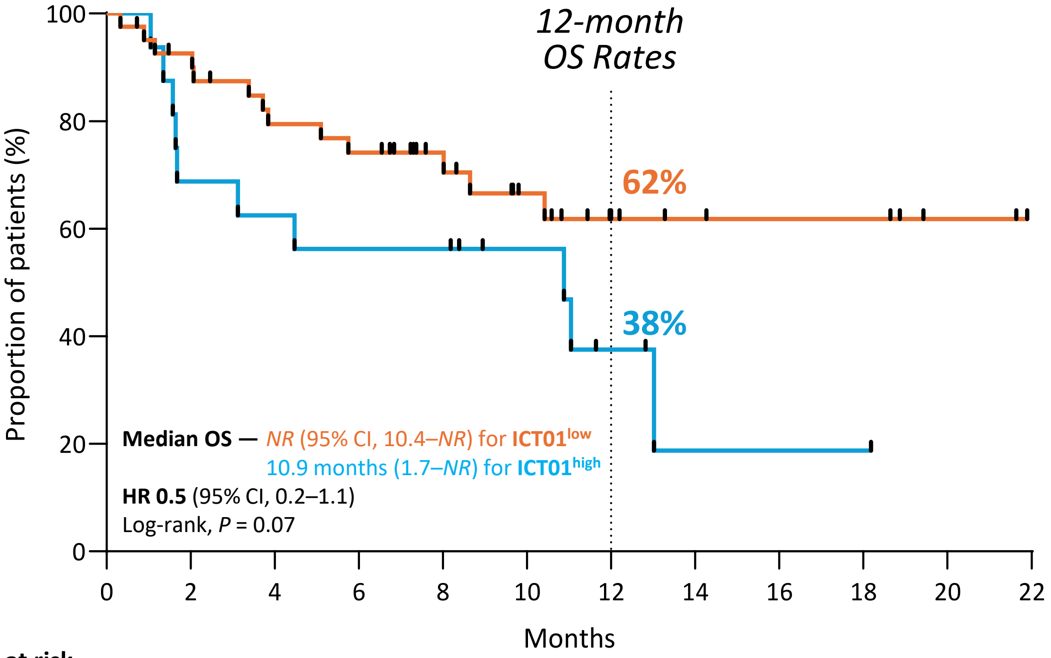
Patients transitioning to SCT — 8 (15%)

Median Duration of Response — ICT01^{low}, *not reached*

ICT01^{high}, 9.3 months

Abbreviations: **SCT**, Stem Cell Transplant; **Follow Up (FU) time** is assessed from the first dose to the last patient contact

Overall Survival



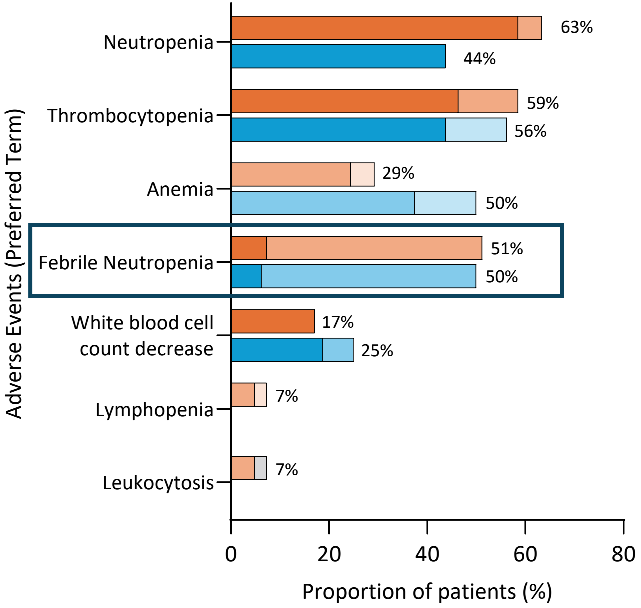
Patients at risk

10 mg	41	36	30	28	20	14	9	6	5	5	2	0
75 mg	16	11	10	9	9	6	3	1	1	1	0	0

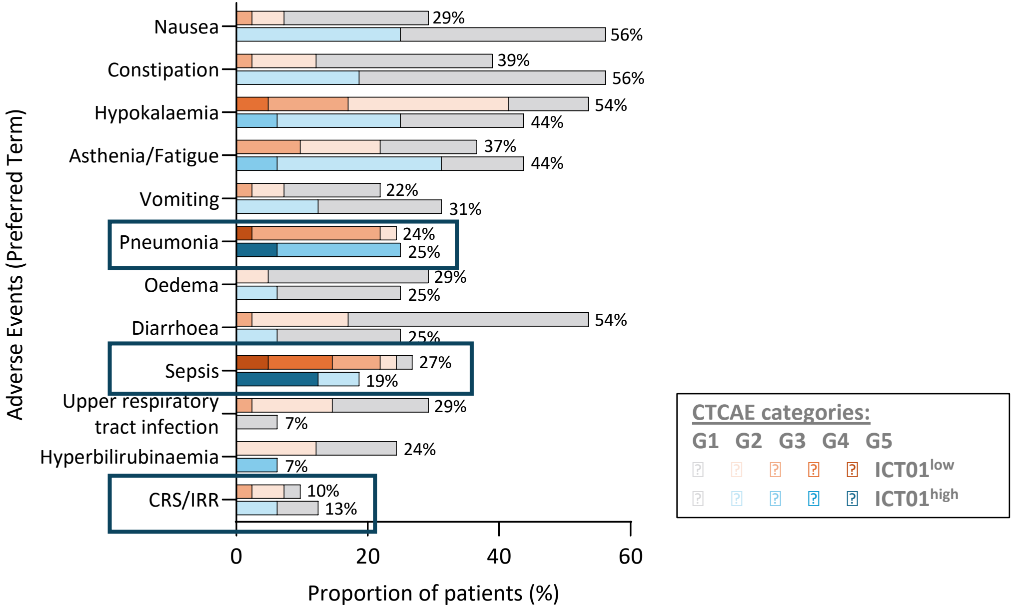
Abbreviations: **NR**, not reached; **OS**, overall survival.

Clinical Safety — Treatment-emergent Adverse Events

Hematological Toxicity



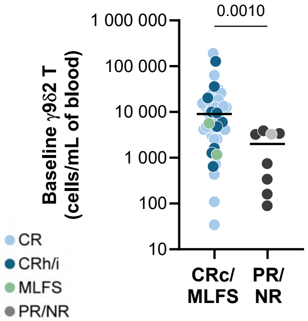
Non-hematological Toxicity



- ⇨ **Hematological toxicity as expected for Ven-Aza-based regimen**
- ⇨ **CRS rate : 10-15% (mainly low grade)**
- ⇨ **Lower incidence of Grade 5 sepsis & pneumonia for ICT01^{low} vs. ICT01^{high}**

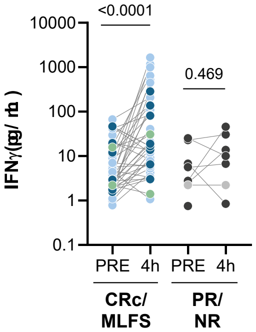
Biomarker/PK analyses (blood samples)

Baseline γ9δ2 T-cell counts



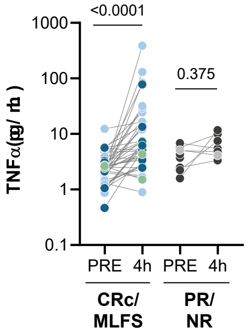
- Non-responders have low baseline γ9δ2 T-cell counts

Serum IFNγ



- ICT01-mediated increase of IFNγ in responders

Serum TNFα



- ICT01-mediated increase of TNFα in responders

⇨ **Non-responders have low baseline γ9δ2 T-cell counts & low-level IFNγ response**
⇨ **γ9δ2 T cells are reliably activated despite the presence of Ven-Aza**
⇨ **ICT01-mediated / cytokine-related bystander activation of NK / CD8 T cells**
⇨ **Individual contribution of ICT01 to the anti-leukemic efficacy of the triplet**

Abbreviations: **NR**, non-responder; **PR**, partial responder;

Conclusions

- ✓ **ICT01^{low}** (10 mg Q4W) ***versus*** **ICT01^{high}** (75 mg Q4W) **in combination with Ven-Aza** has a more favorable benefit-risk profile ⇨ **ICT01^{low} = RP2D**
  - ICT01^{low} is associated with higher CR & CRc rates overall and across molecular AML subtypes
  - ICT01^{low} reveals an early survival signal, suggesting high response rates translate into improved OS
  - ICT01^{low} is clinically very well manageable
  - PD effects support the individual contribution of ICT01^{low} to the improved clinical efficacy
- ✓ ICT01^{low}-Ven-Aza provides higher CR & CRc rate compared to historical control cohort of elderly/unfit AML patients treated with standard Ven-Aza *(data not shown here, subject to future publications)*
- ✓ ICT01-mediated γ9δ2 T-cell activation may emerge as the first immunotherapeutic option for patients with ND AML ineligible for intensive chemotherapy and will be tested in a randomized pivotal study

Acknowledgements & Affiliations

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- All authors contributed to and approved the abstract & the presentation.

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