2025 ASCO® ANNUAL MEETING

γ9δ2 T-cell activation with ICT01 combined with azacitidine-venetoclax for older/unfit adults with newly diagnosed AML: preliminary efficacy and dose selection in Phase 1/2 study EVICTION

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Author and co-author disclosures can be found at ASCO.org

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Key Takeaway Points

1

ICT01^{low}-Ven-Aza generated very high response rates across molecular AML subtypes and is clinically well manageable

2

ICT01 activates γ9δ2 T cells in the presence of Ven-Aza, and the RP2D is 10 mg Q4W (ICT01^{low})

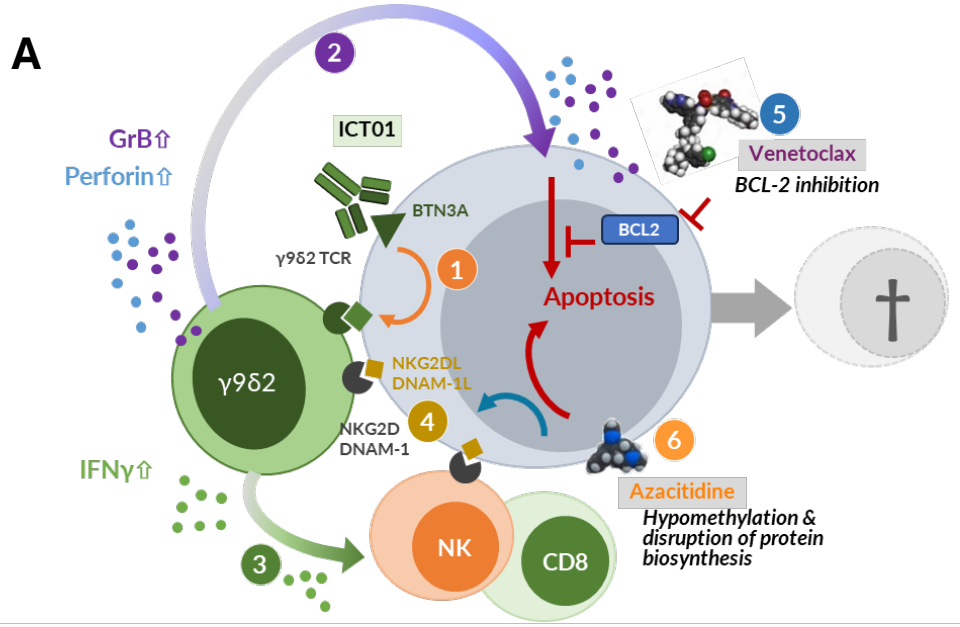
3

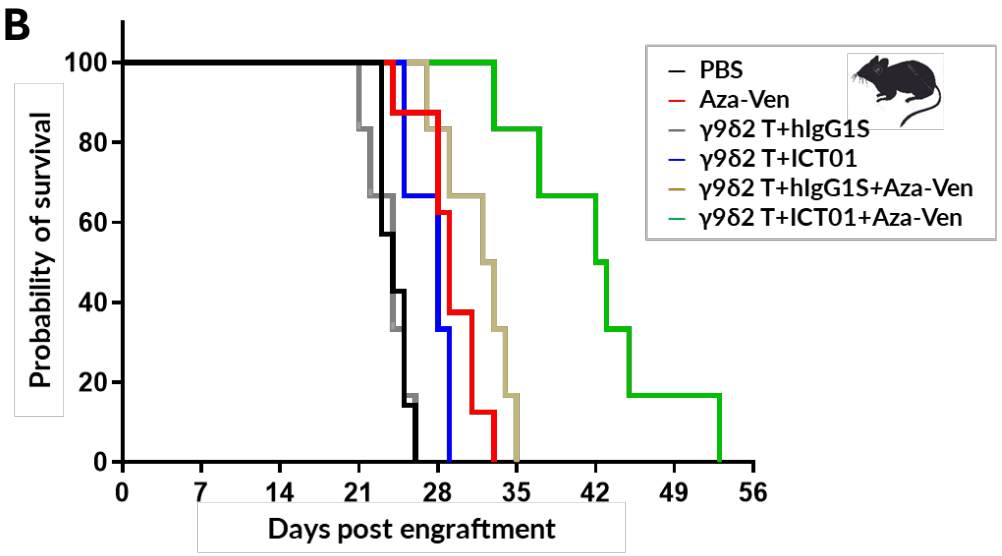
ICT01-mediated γ9δ2 T cell activation may emerge as the first immunotherapeutic option for newly diagnosed AML patients ineligible for induction chemotherapy

Abbreviations: **ICT01^{low}**, 10 mg ICT01 (humanized anti-butyrophilin 3A monocloncal antibody) every 4 weeks; **RP2D**, recommended Phase 2 dose; **Ven-Aza**, venetoclax-azacitidine (standard dosing schedule).

Background

- γ9δ2 T cells are known to drive graft-versus-leukemia efficacy.
- ICT01 is an anti-BTN3A mAb that selectively activates γ9δ2 T cells & triggers cytotoxicity (Panel **A**)
- ICT01-activated γ9δ2 T cells promote anti-leukemic cytotoxicity and immunomodulation
- ICT01-Ven-Aza showed synergistic anti-leukemic efficacy *in vivo* (MOLM-14 mouse model; Panel **B**)
- ICT01 monotherapy was safe, tolerable at 0.7–75 mg ICT01 & modestly effective in R/R phase1 patients



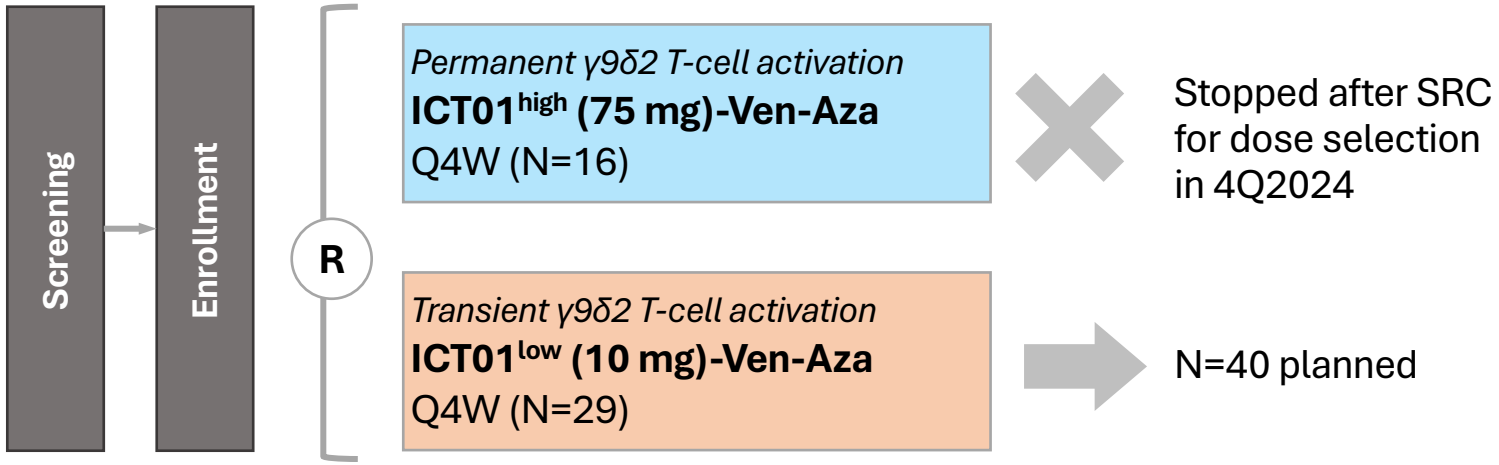


Methods – Dose-optimizing, efficacy-estimating Phase 1 cohorts

Patients with newly diagnosed AML ineligible for intensive chemotherapy/HSCT

Exclusion of patients with:

- Eligible for intensive chemotherapy/HSCT
- t(15;17), t(8;21), inv(16), or t(16;16)
- Prior MPN, PV, CML or AML with tBCR-ABL1.
- Prior Ven exposure
- Systemic corticosteroids in last 28 days
- Active auto-immune disease



- **Interim analysis:** ICT01^{high} stopped based on pharmacodynamic findings following SRC meeting
- **Safety Population (N=45)**: all patients that received at least one dose
- **Efficacy Population (N=39)**: evaluable for efficacy with informative disease/bone marrow assessments
  - Primary Endpoint: ***CR rate*** per European LeukemiaNet 2022 criteria
  - Secondary Endpoints: CRc, OS, EFS, safety, pharmacokinetics, pharmacodynamics (MRD is explored)

Abbreviations: **CR**, complete response; **CRc**, composite CR (CR+CRi+CRh); **HSCT**, hematopoietic stem cell transplantation; **SRC**, Safety Review Committee (meeting); **Ven-Aza**, venetoclax-azacitidine.

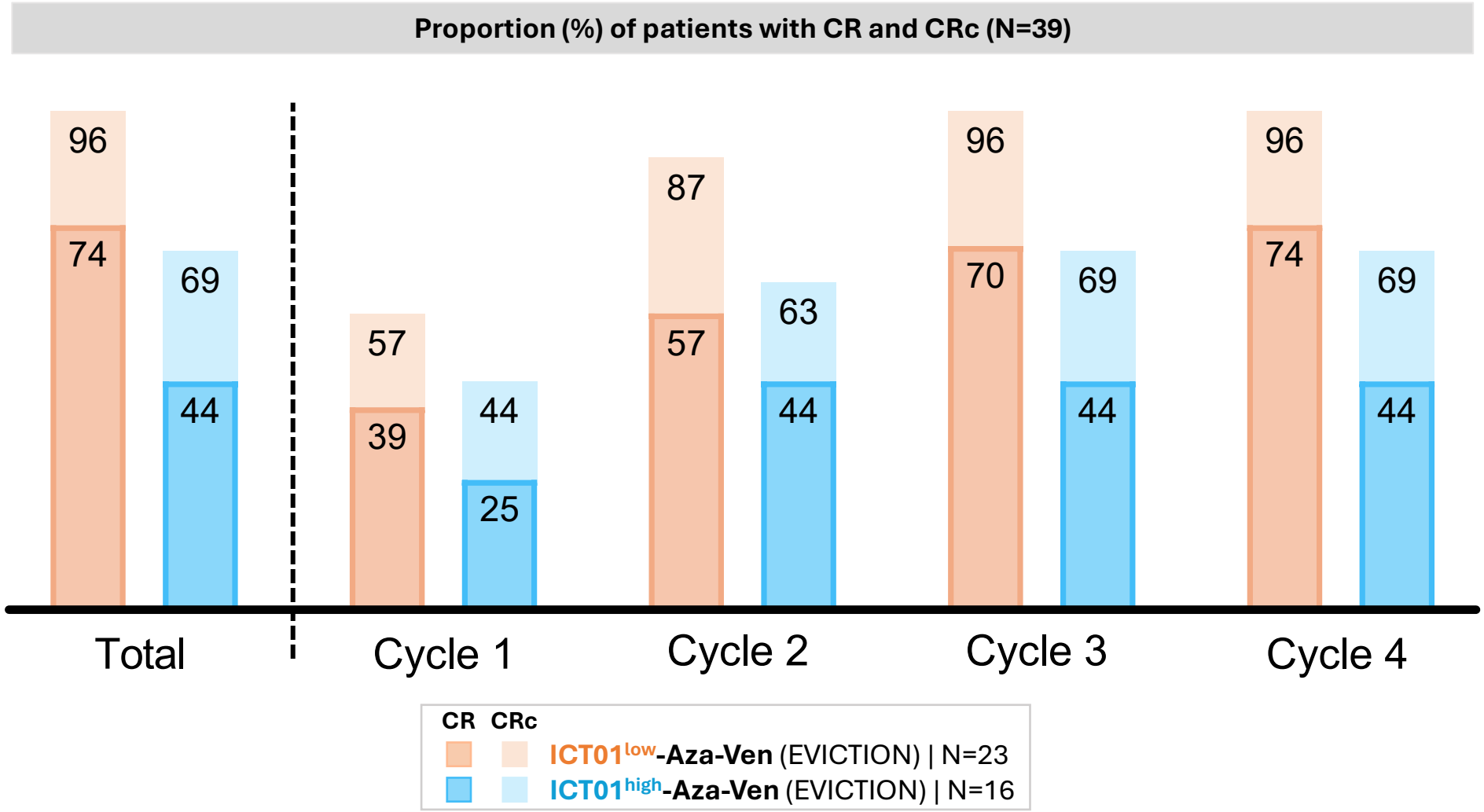
Patient Demographics

Variables	ICT01^{low}-Ven-Aza (N=29)	ICT01^{high}-Ven-Aza (N=16)	Pooled (N=45)
Age [median (range)]	76 (51-87)	75 (64-84)	76 (51-87)
≥ 75 years [n(%)]	17 (59)	9 (56)	26 (58)
Male [n(%)]	17 (59)	7 (44)	24 (53)
ECOG performance status ≥ 2 [n(%)]	5 (17)	6 (38)	11 (25)
Secondary AML* (AML-MR)	10 (34)	6 (38)	16 (36)
Bone marrow blasts [% (range)]	40 (7-98)	34.5 (9-82)	40 (7-98)
< 30 %	12 (41)	8 (50)	20 (44)
≥ 30-50%	8 (28)	2 (12)	10 (22)
≥ 50%	9 (31)	6 (38)	15 (33)
Mutations (multiple entries possible)			
TP53	6 (21)	9 (56)	15 (33)
IDH2	7 (24)	0	7 (16)
NPM1	3 (10)	3 (19)	6 (13)
DDX41	4 (14)	0	4 (9)
ASXL1	4 (14)	1 (6)	5 (11)
FLT3-ITD	1 (3)	0	1 (2)
KRAS	0	2 (13)	2 (4)
NRAS	1 (3)	2 (13)	3 (7)
Refined ELN risk 2024 [n(%)]†			
Favorable	14 (48)	2 (13)	16 (36)
Intermediate	9 (31)	3 (19)	12 (27)
Adverse	6 (21)	11 (69)	17 (38)

*Secondary AML includes therapy related, prior MDS and AML-MR | †Lachowiez et al. Blood 2024:144(26):2788–92.
Abbreviations: **ELN,** European Leukemia Network; **ICT01$^{low/high}$,** ICT01 10 mg/75 mg Q4W; **Ven-Aza**, azacitidine-venetoclax combination treatment.

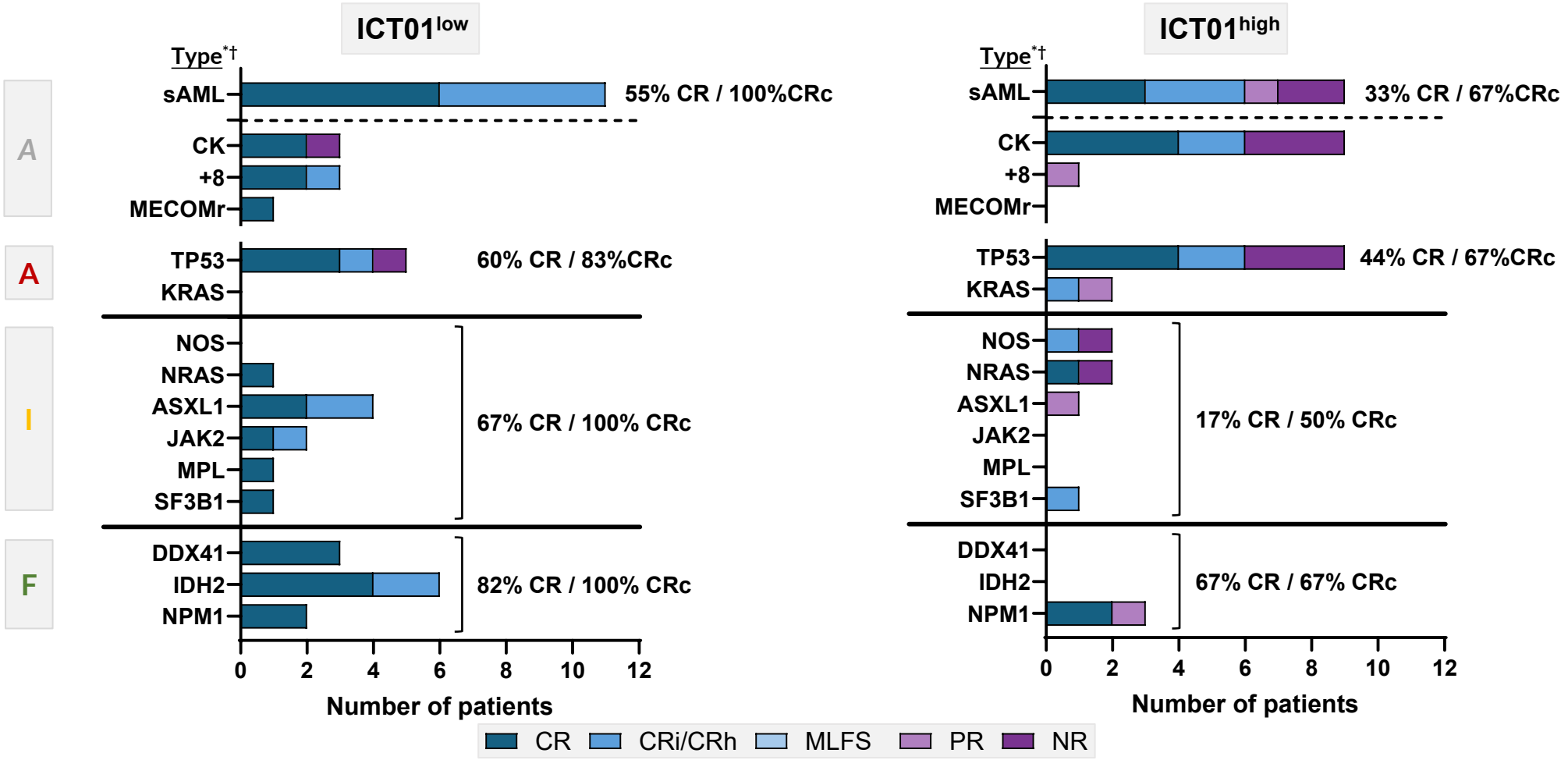
Results – Clinical Efficacy of ICT01-Ven-Aza

ICT01^{low} — 7 of 9 patients (77%) were MRD-negative | ICT01^{high} — 3 of 7 patients (43%) were MRD-negative



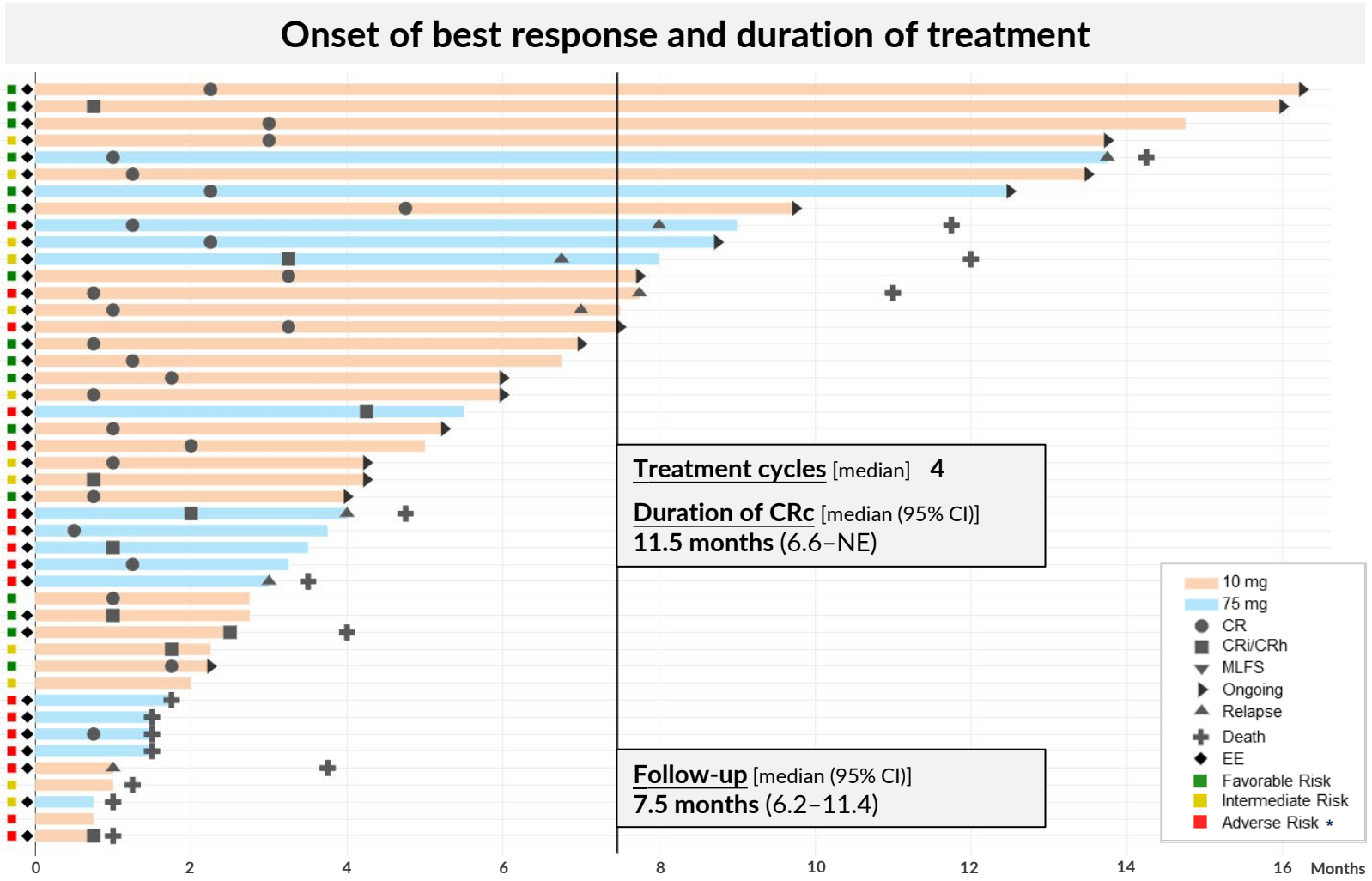
PRESENTED BY: Pierre-Yves Dumas, MD, PhD

Results – Clinical Efficacy by Molecular Subtypes



*Secondary AML includes therapy related, prior MDS and AML-MR, and mutations | †Multiple entries possible due to multiple aberrations | #Refined ELN 2024 per Lachowiez et al. Blood 2024:144(26):2788–92.
Abbreviations: **A/I/F**, adverse/intermediate/favorable risk category; **CR**, complete response; **CRc**, composite CR (CR+CRh+CRi); **MLFS**, morphologic leukemia-free state; **NR**, non-response reported; **PR**, partial remission; **sAML**, secondary AML; **Ven-Aza**, venetoclax-azacitidine.

Results – Clinical Efficacy- Durable responses

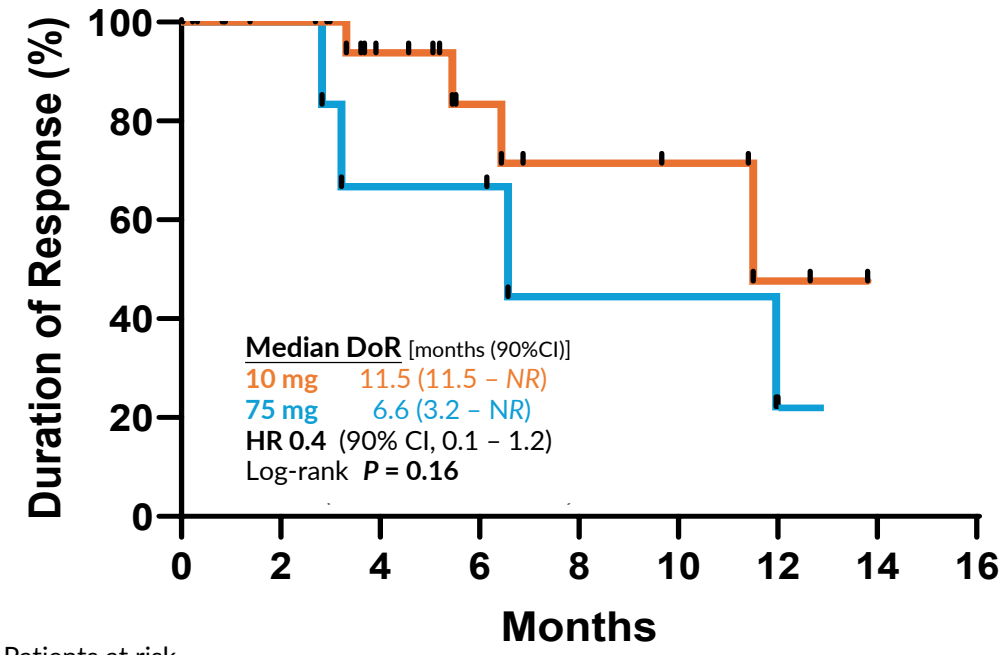


* Refined ELN 2024 per Lachowiez et al. Blood 2024:144(26):2788–92.

Abbreviations: **CR**, complete remission; **CRc**, composite complete remission (CR+CRh+CRi); **EE**, Efficacy Population; **ICT01$^{low/high}$**, 10 mg/75 mg ICT01 Q4W; **Ven-Aza**, venetoclax-azacitidine

Results – Preliminary Response Duration & Overall Survival

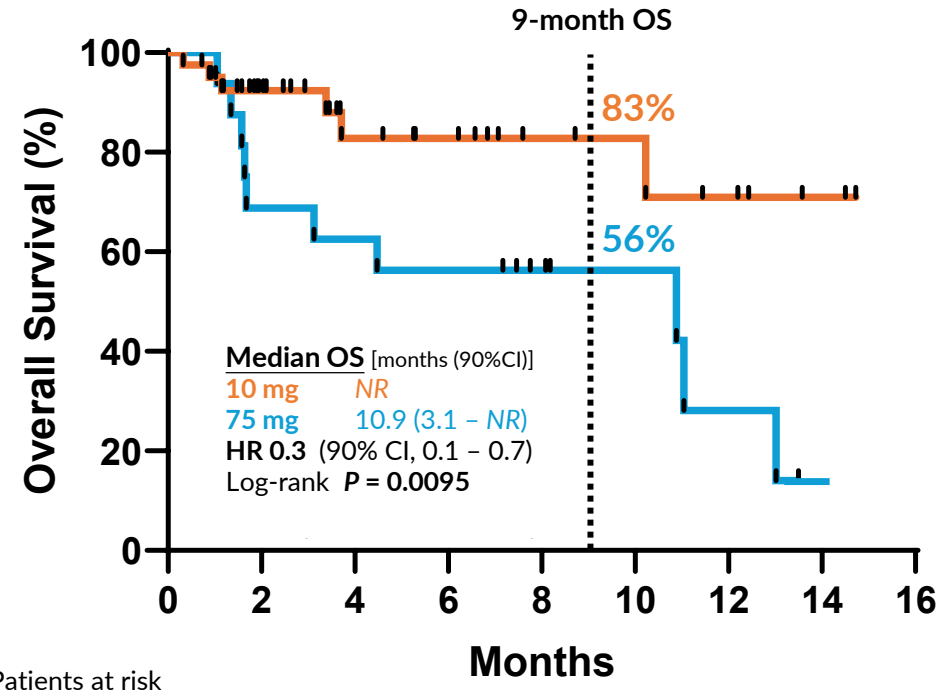
Duration of CRc Response (N=33)



Patients at risk

10 mg	22	19	12	7	5	4	2	0
75 mg	11	7	4	4	2	1	1	0

Overall Survival (N=45)

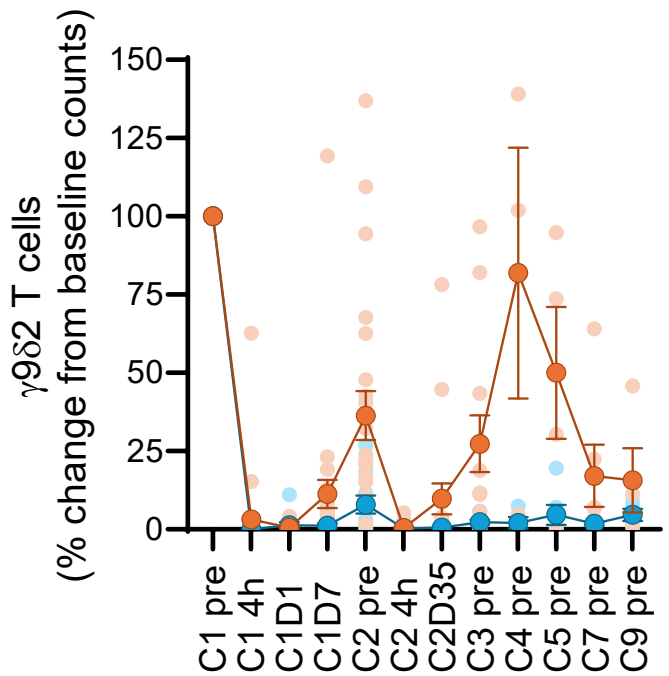


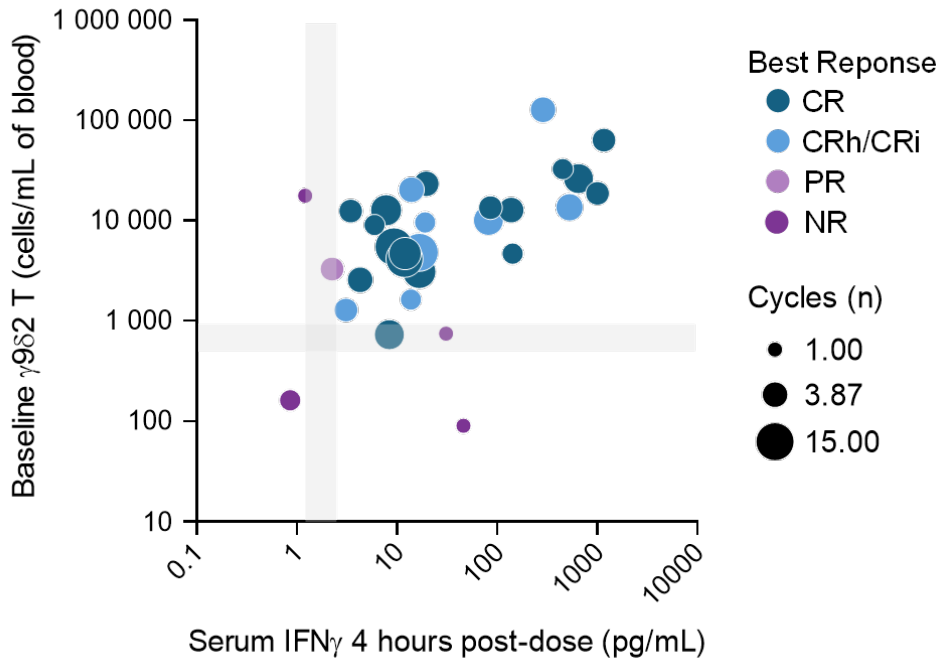
Patients at risk

10 mg	29	24	16	13	8	7	5	2
75 mg	16	11	10	9	6	4	1	1

Abbreviations: **CI**, confidence interval; **DoR**, duration of response; **HR**, hazard ratio; **NR**, not reached; **OS**, overall survival.

Results – Pharmacodynamics





- **Repeated dosing with ICT01^{low} allows for γ9δ2 T-cell recovery**
- **Repeated dosing with ICT01^{high} induces depletion of γ9δ2 T cells, suggestive of activation-induced cell death**

⇨ICT01^{low}(10 mg Q4W) identified as RP2D

- **CR/CRc patients cluster among normal γ9δ2 T-cell counts and strong IFNγ response post-dose.**
- **NR patients have very low baseline γ9δ2 T-cell counts and/or low-level IFNγ response post-dose.**

⇨Evidence for ICT01-mediated efficacy contribution

Abbreviations: **CI**, confidence interval; **NR**, non-responder; **RP2D**, recommended Phase 2 dose.

Results – Patient Safety

New or worsening laboratory abnormalities or TEAEs occurring in ≥10% of patients (or Grade ≥ 3 in ≥ 2 patients) treated with ICT01-Aza-Ven (N=45)

Laboratory values or TEAEs	All Grades		Grade ≥ 3	
	ICT01^{low}+AV (N=29) *[N (%)]*	ICT01^{high}+AV (N=16) *[N (%)]*	ICT01^{low}+AV (N=29) *[N (%)]*	ICT01^{high}+AV (N=16) *[N (%)]*
Hematology (laboratory values only)				
Neutrophils decreased	27 (93)	14 (88)	26 (90)	14 (88)
Platelets decreased	24 (83)	12 (75)	19 (66)	11 (69)
Lymphocytes decreased	26 (90)	15 (94)	18 (62)	13 (81)
Hemoglobin decreased	20 (69)	13 (81)	12 (41)	12 (75)
Blood system disorders				
Febrile neutropenia	13 (45)	8 (50)	13 (45)	8 (50)
Gastrointestinal disorders				
Constipation	12 (41)	9 (56)	1 (3)	0
Diarrhea	13 (45)	4 (25)	0	0
Nausea	11 (38)	9 (56)	0	0
Vomiting	7 (24)	4 (25)	0	0
General disorders				
Asthenia/fatigue	9 (31)	7 (44)	1 (3)	1 (6)
Infections and infestations				
Sepsis/bacteremia	8 (28)	3 (19)	8 (28)	2 (13)
Pneumonia	4 (14)	4 (25)	4 (14)	4 (25)
Chemistry (laboratory values only)				
Bilirubin increased	13 (45)	4 (25)	0	0
AP increased	10 (34)	3 (19)	0	0

Early mortality*

- 30-day: **4%**

Days between cycles [median (IQR)]

- C1D1 to C2D1: **30d** (28,37)
- C2D1 to C3D1: **30d** (28,40)
- C3D1 to C4D1: **28d** (28,42)
- C4D1 to C5D1: **28d** (28,46)

CRS

First patient had CRS Grade 3

⇨ Dexamethasone prophylaxis implemented by SRC

⇨ Incidence: 9% (all Grade 1 or 2)

*To date, all fatal events assessed by the investigator as '*unlikely related/unrelated to ICT01*' (confirmed by SRC review; plausibility confirmed by ImCheck).

Abbreviations: **C**, cycle; **D**, day; **d**, days; **IQR**, interquartile range; **SRC**, Safety Review Committee.

Conclusions

- ICT01^{low} *vs.* ICT01^{high} in combination with Ven-Aza generated higher CR rates across molecular AML subtypes.
- ICT01^{low}-Ven-Aza is clinically well manageable.
- γ9δ2 T cells are reliably activated in the presence of Ven-Aza.
- 10 mg ICT01 Q4W has a favorable benefit-risk profile and is selected as RP2D.
- Differential OS of ICT01^{low} *vs.* ICT01^{high} suggests potential translation of high CR / CRc / CRc$_{MRD-}$ rates into improved OS.
- γ9δ2 T-cell activation may emerge as a first immunotherapeutic option for AML and will be tested in a randomized clinical study.

Acknowledgements

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

Lay Summary

- **What did this research tell us?**
  γ9δ2 T cells as part of the human immune system can be stimulated to help treating AML and appear to be very effective and safe
- **Who does this research impact?**
  The novel frontline regimen ICT01-Ven-Aza may help to improve the treatment outcomes of patients with newly diagnosed AML elderly and/or too sick to receive standard chemotherapy.
- **What does this mean for patients right now?**
  - **ICT01 is not an approved treatment for AML and currently not available outside of clinical studies.**
  - **Patients newly diagnosed with AML and interested in treatment options with ICT01 may participate in future studies with ICT01-Ven-Aza.**