Durable Responses and Survival in High Risk AML and MDS Patients Treated With an Allogeneic Leukemia-derived Dendritic Cell Vaccine

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BACKGROUND

Maintenance of induced responses is of unmet need in AML or MDS patients not eligible for allogeneic stem cell transplantation (allo-SCT). To accomplish this, immune therapeutic strategies are emerging. **DCP-001** is an allogeneic leukemia-derived dendritic cell vaccine that aims to prevent or delay relapse. In this phase 1 study in AML in CR1/2 or relapse/refractory disease not eligible for allo-SCT a bi-weekly vaccination was evaluated.

AIM OF THE STUDY

To identify parameters that correlate with long-term survival from the DCP-001 phase 1 clinical study (NCT01373515)[1]

RESULTS

Patient cohort: total n=12; n=7 responders*; n=5 non-responders.

Response is defined as decreased or stable morphologic blast counts in bone marrow at day 126 (primary endpoint of study) compared to study entry.

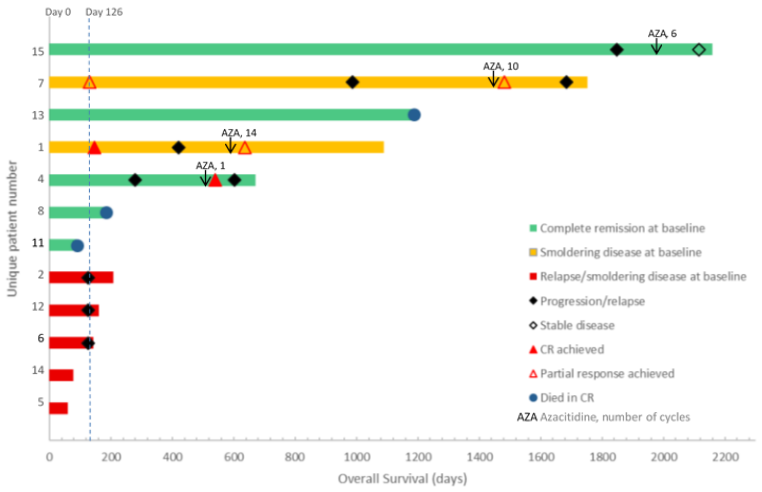

Figure 1. Swimmer's plot showing long-term follow-up data upon DCP-001 phase 1 trial.
Day 0 represents start date of study evaluation; first vaccination was given

RESULTS

1. Long-term survival was correlated to response (figure 1)
- Median OS responders: 1090 days (range 90-2160)
- Median OS non-responders: 144 days (range 59-209)

2. Response was associated with: (figure 1, table 1)
- CR of disease at study entry
- Short median time between diagnosis and study entry
- No prior treatment other than induction chemotherapy

3. Azacitidine can be applied as rescue therapy upon progression after vaccination (figure 1)

4. Survival differences were not explained by differences in risk score, cytogenetics or age (table 1)
- No difference in risk distribution between responders and non-responders

Table 1. Patient characteristics at study entry DCP-001 phase 1 study

UPN	Age	Diagnosis	NGS / qPCR[a]	Cytogenetics	Risk score[b]	Time between diagnosis and first vaccination (days)	Additional treatment prior to vaccination	Remission status at study entry (Day 0)	OS (days)
Responders									
15	68	RAEB-2	EVI-1, NGS MD	CN-X-Y	High	169	-	CRi-tn	2160
7	74	AML with prior MDS	*NGS MD*	CN-X-Y	Intermediate	422	-	Stable refractory	1752
13	65	AML with prior MDS	*NGS MD*	Y-	Intermediate	105	-	CRi-t	1188
1	66	AML	ASXL1, DNMT3A, IDH2, PHF6, RUNX1, SMC1A	del(17q) monosomy 7	Adverse	240	-	Smoldering	1090
4	72	AML	SRSF2, TET2	CN-X-Y	Intermediate	1398	AZA	CR2i-t	672
8	64	AML with prior MDS	ETV6, IKZF1, PHF6, U2AF1	trisomy 8, del(5q)	Adverse	233	-	CRi-t	184
11	57	RAEB-2	ASXL1	CN-X-Y	High	343	-	CRi-t	90
Non-responders									
2	70	AML	PTPN11, RUNX1	t(1;3), del(5q)	Adverse	219	-	Relapse/ smoldering	209
12	70	RAEB-2	CEBPα-DM, ASXL1, EZH2, NRAS, PTPN11, RUNX1, TET2	trisomy 22	Very high	671	AZA	Relapse/ smoldering	162
6	69	AML	*NGS MD*	CN-X-Y	Intermediate	555	AZA	Relapse/ smoldering	144
14	67	AML	EVI-1, ASXL1, DNMT3A, JAK2, PHF6, RUNX1	CN-X-Y	Adverse	611	AZA	Relapse/ smoldering	79
5	74	AML	*NGS MD*	CN-X-Y	Intermediate	2310	Barasertib[c]; AZA	Relapse/ smoldering	59

Abbreviations: UPN = unique patient number; MDS= Myelodysplastic syndrome; RAEB= refractory anemia with excess of blasts; NGS = next generation sequencing; qPCR = quantitative polymerase chain reaction; MD = missing data; CN-X-Y = normal cytogenetics; CR complete remission, CRi = complete remission with incomplete hematologic recovery; CRi-t = incomplete hematologic recovery based on thrombocytopenia <100x10e9/L; CRi-n = incomplete hematologic recovery based on absolute neutrophil count <1.0x10e9/L); CR2 = second complete remission after relapse; RFS = relapse free survival only depicted for those that were in remission/stable disease at end of study; OS = overall survival

[a]NGS / qPCR: only positive mutations or expressions are depicted. Determined via NGS at the Erasmus Medical Center Rotterdam: ASXL1; DNMT3A; IDH2; PHF6; RUNX1; SMC1A; PTPN11; SRSF2; TET2; ETV6; IKZF1; U2AF1; CEBPα-DM; JAK2 . Determined at the Amsterdam UMC, VU University Medical Center: EVI-1, BCR-ABL, CEBPα, FLT3itd, Inv(16), MLL11q23, NPM1. [b]Risk score retrospectively determined at diagnosis; based on European Leukemia Net cytogenetic risk score in AML patients, and Revised International Prognostic Scoring System (IPSS-R) in MDS patients. [c]Patient DC-005 has had an experimental consolidation therapy in the cohort AZD 1152: 1st cohort CHR-2845-001 phase 1. † died before end of study. †# died before end of study due to infection. # died in complete remission of disease

CONCLUSION / FUTURE PERSPECTIVES

These data support the rationale that DCP-001 may prolong duration of remission or smoldering disease in intermediate and high risk AML and MDS patients.

Important parameters correlated with long-term survival from DCP-001 in the clinical phase 1 study are treatment shortly after achieving complete remission and a shorter time between diagnosis and study entry.

Currently, an international multi-center phase 2 study (ADVANCE II; NCT03697707) is being conducted to determine the effect of DCP-001 in patients with AML in CR but positive for measurable residual disease (MRD+) aiming to convert MRD+ to a MRD- state as primary endpoint.

[1]Van de Loosdrecht, et al. Cancer Immunology, Immunotherapy; 67:1505–1518 (2018)

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Disclosure of conflict of interest Jeroen Rovers is an employee of DCprime. Tanja de Gruijl receives consultancy fees of DCprime as member of the advisory board. For the other authors no conflict of interest is present.