Kiadis Pharma
Clinical Trial Factsheet | Q1 2019

Current Pipeline & Development Status

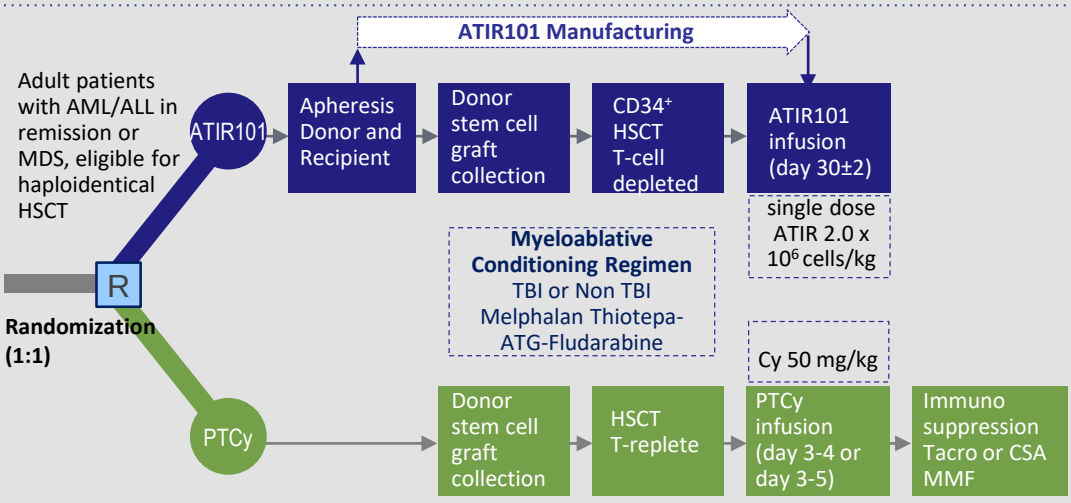
Region	Phase I	Phase II	Phase III	Filing	Catalysts	Commercial Rights	Comments
EU	*Orphan Drug Designation*				• CHMP opinion '19 • EU Launch: one patient, late '19	Kiadis pharma	Received EMA Day 180 2nd List of Issues (9/2018)
US	*Orphan Drug & RMAT Designations*				• Phase 3 interim read out ('21; 105 events)	Kiadis pharma	RMAT 'breakthrough' designation (9/2017; FDA access, priority review, support

All trials: Patients: adult AML/ALL/MDS; **Conditioning**: Myeloablative; **Graft source**: Haplo PBMCs; **HSCT:** T-cell depleted (CD34+); **ATIR:** ~30 days after HSCT; No prophylactic immunosuppression

Phase 3: CR-AIR-009; Single dose ATIR

OBJECTIVE: Demonstrate superior clinical benefit and collect pharmacoeconomic data

Randomized/controlled (ATIR versus PTCy) • Initiated 2017 (enrolling) • 250 patients • Event driven primary endpoint (GRFS) • ~50 sites planned CA, Europe, US, Israel



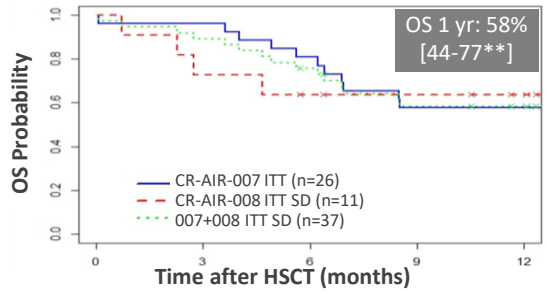
PRIMARY ENDPOINT:
GVHD-Free & Relapse-Free Survival (GRFS): survival without relapse, grade III/IV acute GVHD or chronic GVHD requiring immunosuppression
- Interim analysis: at 2/3 of events (17,6% GFRS treatment effect, hazard ratio 0.61)
- Primary analysis: at 156 events (11,4% GFRS treatment effect, hazard ratio 0.73)

SECONDARY ENDPOINTS:
Overall Survival (OS), Progression Free Survival (PFS), Relapse, Non Relapse Mortality (NRM)

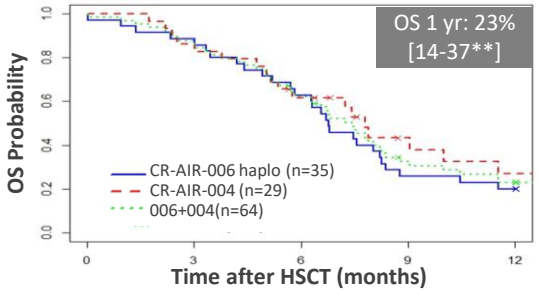
OTHER:
Randomized at enrollment; Balanced conditioning regimens in ATIR/PTCy arms; Stratification for Disease Risk Index, underlying disease and treatment site

Phase 2: CR-AIR-007/008/006/004; Improved Overall Survival (ITT*, Single Dose; 1 yr) P=0.005

T-cell depleted HSCT *with* ATIR101 (n=37)



T-cell depleted HSCT *without* ATIR (n=64)



*ITT (intention to treat): all patients undergoing T-cell depleted CD34+ HSCT; SD: single dose; CR-AIR-008 status 1 June 2018 (3 patients at risk); ** 95% confidence interval

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Phase 2 Studies in AML/ALL/MDS

CR-AIR-007: Single dose ATIR

- Open label single arm; 2013-2018
- 23/26 patients (MITT/ITT*)
- 2 year follow up
- Sites in BE, CA, GE, UK

CR-AIR-008: Single dose ATIR and two doses ATIR**

- Open label single arm; 2015-2018 (ongoing)
- 9/11 single dose; 6/6 patients two doses (MITT/ITT)
- 3 patients still at risk
- 1 year follow up
- Sites in CA, BE, GE, UK

CR-AIR-004: Historical Control, No ATIR

- Open label single arm; 2009-2012
- 40 patients (29 matched to CR-AIR-007)
- Sites in BE, CA, GE, NL, UK, US

CR-AIR-006: Historical Control, No ATIR

- Observational cohort, EBMT registry; 2006-2013
- 35 patients (all matched to CR-AIR-007)
- 1 year follow up

* MITT: Modified Intent to Treat (transplanted and ATIR); ITT: Intent to Treat (transplanted); ** CR-AIR-008 was designed to test safety of second dose, but due to higher then expected GVHD it was decided to stop infusing second dose (in accordance with protocol)

ATIR Phase 2 Data	T-cell depleted (CD34+) *with* single dose ATIR (n=37)*			T-cell depleted (CD34+) *without* ATIR (n=64)*		
	CR-AIR-007	CR-AIR-008	007-008	CR-AIR-006	CR-AIR-004	004-006
1 year post HSCT	**(ITT n=26)**	**(ITT n=11)**	**(ITT n=37)**	**(n=35)**	**(n=29)**	**(n=64)**
Overall Survival	58% (42-80)	64% (41-100)	58% (44-77)	20% (10-39)	27% (13-54)	23% (14-37)
Non-relapse mortality	35%	27%	33%	66%	59%	63%
Relapse-related mortality	8%	9%	8%	15%	14%	14%
Relapse	8%	9%	8%	NA	NA	NA
Acute GVHD grade II-IV	19%	27%	21%	20%	18%	19%
Acute GVHD grade III-IV	0%	18%	5%	6%	7%	6%
Chronic GVHD	4%	0%	3%	11%	5%	8%
Chronic GVHD severe	0%	0%	0%	9%	5%	7%
6mths post HSCT	**(MITT n=23)**	**(MITT n=9)**	**(MITT n=32)**	**(n=35)**	**(n=29)**	**(n=64)**
Non-relapse mortality	13% (0-27)	11% (0-29)	13% (0-24)	37% (19-51)	35% (15-51)	36% (23-47)

*Notes: NRM at 6 months primary endpoint of CR-AIR-007; Kaplan-Meier estimates for OS and NRM at 6 months; all other estimates cumulative incidence analyses; ITT: patients receiving HSCT; MITT: patients receiving HSCT and ATIR; OS: overall survival; CR-AIR-008 status 1 June 2018 (3 patients at risk);
All trials: Conditioning: Myeloablative; Graft source: Haplo PBMCs; HSCT: T-cell depleted; ATIR: ~30 days after HSCT; No prophylactic immunosuppression

ATIR101 Compared to PTCy Literature Studies (basis for phase 3 design)

1-year Patient Outcomes after T-cell Depleted Haplo-HSCT with ATIR101 or T-Cell Replete HSCT with PTCy

Average	ATIR101 (Two phase 2 trials: N=37; ITT)	PTCy[λ]	
Relapse	8%	25%	N=2579[5,8,10-32]
RRM	8%	14%[ϒ]	N=2384[5,8,10-29,31-33]
NRM	33%	22%	N=1996[5,10-29,31-33]
aGVHD (grade III/IV)	5%[*]	8%[ξ]	N=1419[5,10-13,16-22,25-30]
cGVHD	3%	22%	N=1312[5,10,12-14,16-22,24-27,29,31]
OS	58%	64%	N=2384[5,8,10-29,31-33]

*All grade III aGHVD. †Data are weighted by number of patients in each of the PTCy publications with >50% AML/MDS/ALL. ‡Calculated as RRM = (100 - OS) – NRM; note that the N-value for NRM was lower (N=1996) than for OS (N=2384). §Day 100 grade III/IV aGVHD.

1-year GRFS after T-cell Depleted Haplo-HSCT with ATIR101 or T-Cell Replete Haplo-HSCT with PTCy

Average	ATIR101	PTCy studies	
	Two phase 2 trials (N=37)	Johns Hopkins (N=372)	Northside (N=128)
DRI	L: 0% I: 57% H: 43%	L: 14% I: 67% H: 19%	L: 19% I: 39% H: 40%
1 yr GRFS (95% CI)	53% (39-72)[π]	45% (40-50)	33% (25-41)
DRI adjusted 1 yr GRFS[α]	53% (39-72)[π]	40%	30%

*Kaplan–Meier estimate of 1-year GRFS in 37 patients in the ATIR101 studies; [π]Normalized according to the DRI profile in the ATIR101 clinical trials population to allow comparison.; H, high and very high; I, intermediate; L, low

PTCy Literature References: 5. Ciurea SO, et al. Blood 2015; 126: 1033–1040; 8. McCurdy SR, et al. Haematologica 2017; 102:391–400; 10. Devillier R, et al. ASBMT Abstracts 2015; 6:8388–8396; 11. Di Stasi A, et al. Biol Blood Marrow Transplant 2014; 20:1975–1981; 12. Ciurea SO, et al. Biol Blood Marrow Transplant 2012; 18:1835–1844; 13. Solomon SR, et al. Biol Blood Marrow Transplant 2012; 18:1859–1866; 14. Esquirol A, et al. Bone Marrow Transplant 2016; 51:S314–S513; 15. Piemontese S, et al. J Hematol Oncol 2017; 10:24; 16. Sugita J, et al. Biol Blood Marrow Transplant 2015; 21:1646–1652; 17. Kanate AS, et al. Blood 2016; 127:938–947; 18. Bashey A, et al. Biol Blood Marrow Transplant 2016; 22:125–133; 19. Slade M, et al. Biol Blood Marrow Transplant 2017; 23:1736–1743; 20. Kasamon YL, et al. Blood Adv 2017; 1:288–292; 21. Fraccaroli A, et al. Am J Hematol 2018; Epub ahead of print; 22. Baker M, et al. Biol Blood Marrow Transplant 2016; 22:2047–2055; 23. Carnevale-Schianca F, et al. Biol Blood Marrow Transplant 2017; 23:459–466; 24. Kwon M, et al. Bone Marrow Transplant 2017; 52:1138–1143; 25. Ruggeri A, et al. Haematologica 2017; 102:401–410; 26. Srour SA, et al. Biol Blood Marrow Transplant 2017; 23:318–324; 27. Devillier R, et al. Bone Marrow Transplant 2016; 51:194–198; 28. Duléry R, et al. Biol Blood Marrow Transplant 2018; 24:1013–1021; 29. Gaballa S, et al. Cancer 2016; 122:3316–3326; 30. Lorentino F, et al. Blood Adv 2017; 1:669–680; 31. Rashidi A, et al. Bone Marrow Transplant 2016; 51:1561–1564; 32. Robin M, et al. Biol Blood Marrow Transplant 2018; Epub ahead of print; 33. Robin M, et al. Blood Adv 2017; 1:1876–1883; 34. Santoro N, et al. J Hematol Oncol 2017; 10:113; 35. Rovers J, et al. EBMT 2017; poster presentation #A171; 36. Clinicaltrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT02999854 (accessed November 2018).