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AFM-13 in PTCL

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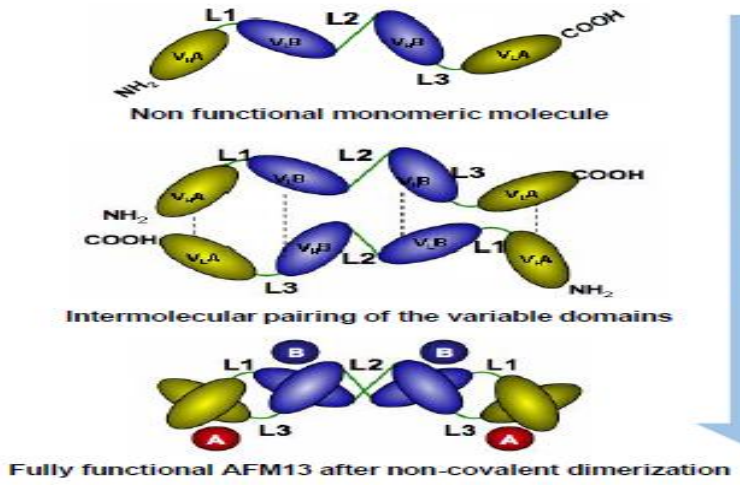
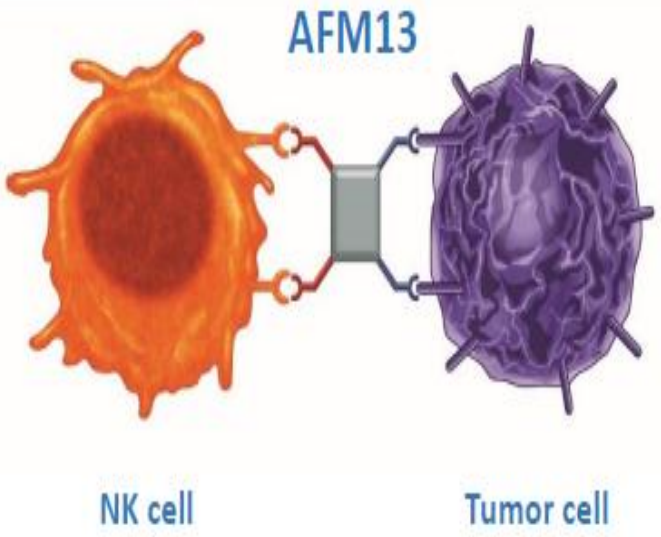
AFM13 (CD16A/CD30): innate cell engager



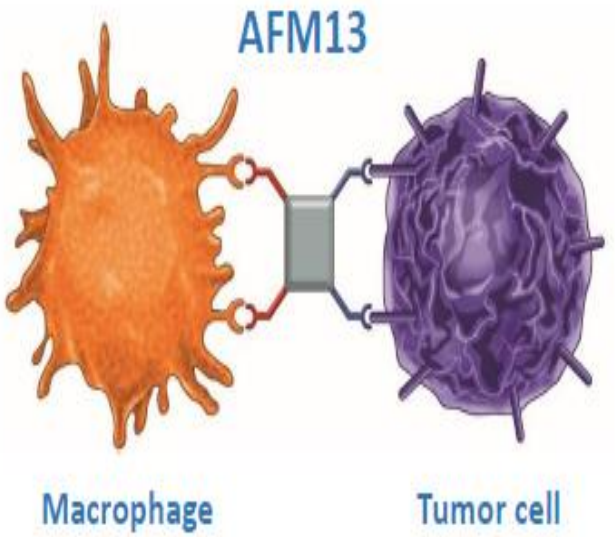
A) Anti-CD16A (FcγRIIIA)
- Human, derived from Affimed's antibody library
- Specific for A isoform of FCγRIII on NK cells and macrophages

B) Anti-CD30
- Murine, derived from Hybridoma HRS-3

MOA: Antibody-dependent cellular cytotoxicity (ADCC) by NK cells



MOA: Antibody-dependent cellular phagocytosis (ADCP) by macrophages



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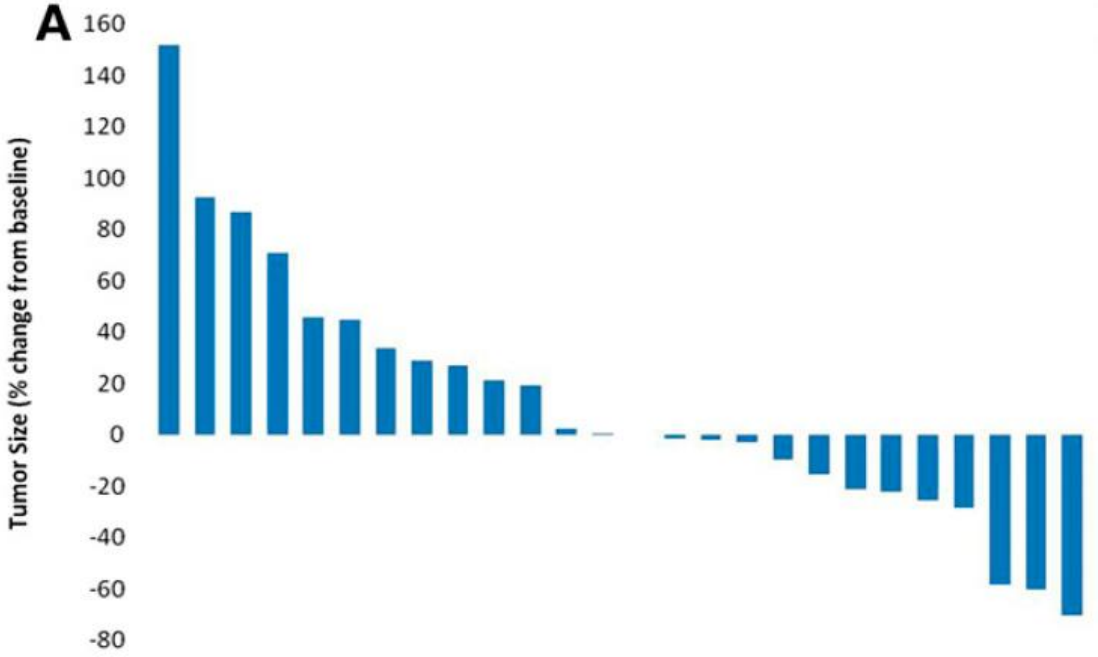
AFM13 in R/R HL

System organ class and preferred term	Cohort 1: 0.01 mg/kg (n = 3)	Cohort 2: 0.04 mg/kg (n = 3)	Cohort 3: 0.15 mg/kg (n = 3)	Cohort 4: 0.5 mg/kg (n = 6)	Cohort 5: 1.5 mg/kg (n = 3)	Cohort 6: 4.5 mg/kg (n = 3)	Cohort 7: 7 mg/kg (n = 3)	Cohort 8: 2 × 4.5 mg/kg (n = 4)	Overall (n = 28)
Any AE of CTCAE grade ≥3	0	0	0	1 (16.7)	3 (100.0)	1 (33.3)	2 (66.7)	1 (25.0)	8 (28.6)
Blood and lymphatic disorders									
Anemia	0	0	0	1 (16.7)	0	1 (33.3)	0	0	2 (7.1)
Hemolytic anemia	0	0	0	1 (16.7)	0	0	0	0	1 (3.6)
Thrombocytopenia	0	0	0	1 (16.7)	0	0	0	0	1 (3.6)
General disorders									
Multiorgan failure	0	0	0	1 (16.7)	0	0	0	0	1 (3.6)
Pyrexia	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
Thrombosis in device	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
Infections and infestations									
Bronchitis	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
Pneumonia	0	0	0	1 (16.7)	1 (33.3)	0	1 (33.3)	1 (25.0)	4 (14.3)
Staphylococcal infection	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
Investigations									
Bilirubin increased	0	0	0	1 (16.7)	0	0	0	0	1 (3.6)
Metabolism and nutrition									
Hypoalbuminemia	0	0	0	1 (16.7)	0	0	0	0	1 (3.6)
Neoplasms									
T-cell lymphoma	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)

Rothe A wr al Blood 2015

AFM13 in R/R HL

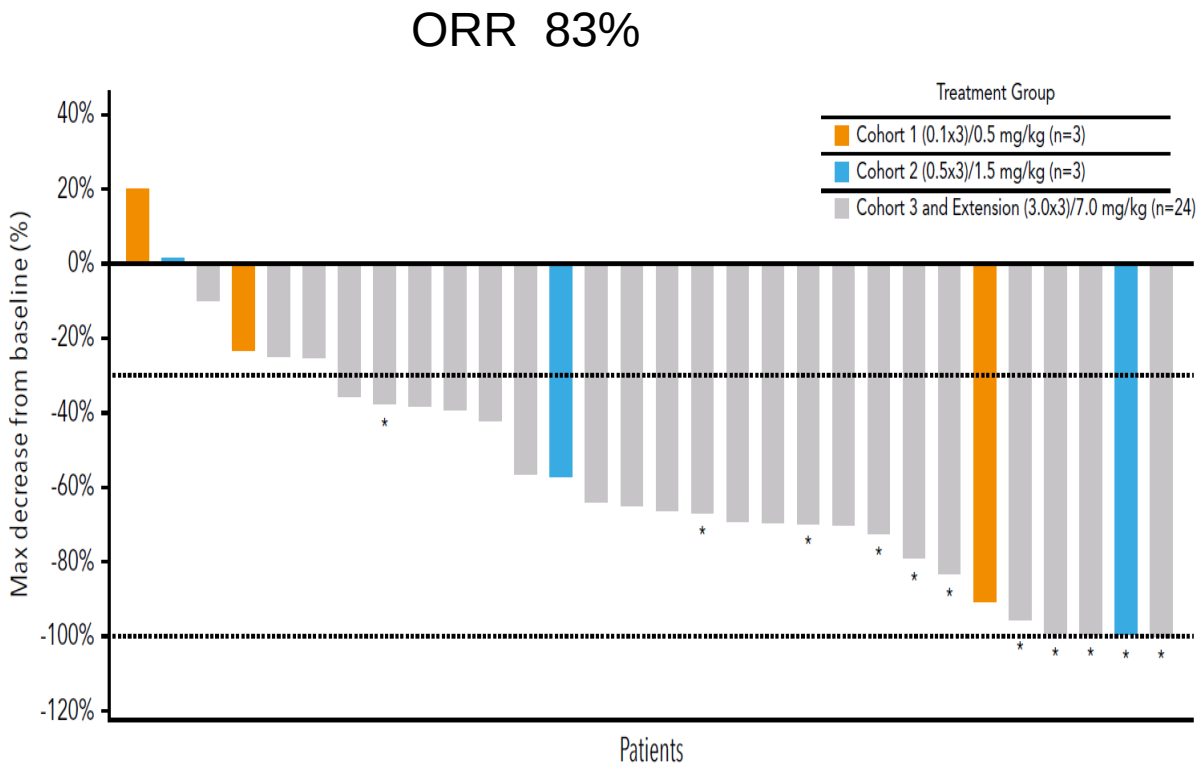
Best response to AFM13, efficacy population (n = 26)	Patients, n (%)
Complete remission	0 (0.0)
Partial response	3 (11.5)
Stable disease	13 (50.0)
Progressive disease	10 (38.5)
Disease control rate	61.5



Rothe A wr al Blood 2015

AFM13+pembrolizumab

	AFM13 dose levels (mg/kg)			Pembrolizumab (mg)
	Weeks 2 and 3	Weeks 4-9	Weeks 10, 13, 16, 19, 22, 25	Weeks 1-52 Q3W*
Cohort 1	0.1 × 3	0.5	0.5	200
Cohort 2	0.5 × 3	1.5	1.5	200
Cohort 3	3.0 × 3	7.0	7.0	200



Pt with prior anti-PD1, Anti-PDL1, anti-PDL2 were excluded.

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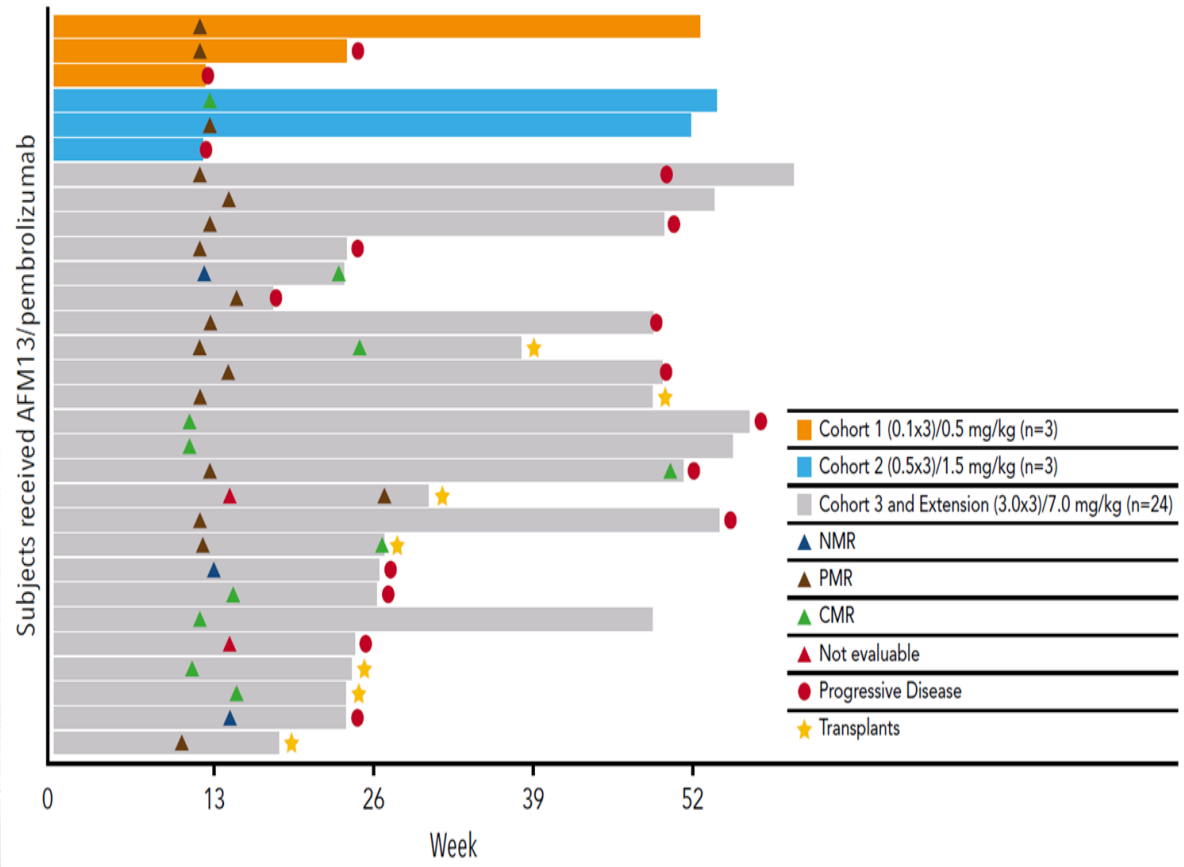
AFM13+pembrolizumab



	CMR, n (%)	PMR, n (%)	NMR, n (%)	PD, n (%)	ORR, n (%)
Investigator assessment					
Cohorts 1 and 2 (n = 6)	1 (17%)	3 (50%)	0 (0%)	2 (33%)	4 (67%)
Cohort 3 and extension (n = 24)	10 (42%)	11 (46%)	2 (8%)	1 (4%)	21 (88%)
Safety analysis set (n = 30)	11 (37%)	14 (47%)	2 (7%)	3 (10%)	25 (83%)
Investigator assessment					
Cohorts 1 and 2 (n = 5)	1 (20%)	2 (40%)	2 (40%)	0 (0%)	3 (60%)
Cohort 3 and extension (n = 24)	11 (46%)	10 (42%)	0 (0%)	3 (13%)	21 (88%)
Safety analysis set (n = 29)	12 (42%)	12 (42%)	2 (7%)	3 (10%)	24 (83%)

Median response duration : in all responders 9.9 months (95% CI, 8.4-not estimable [NE]),
in CR 10.4 months (95% CI, 2.8-10.4),

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AFM13 monotherapy in patients with CD30+lymphoma

CD30-Positive Lymphoma

Phase 1b/2a Trial:

- Investigator-sponsored*, translational study to evaluate immunological effects and preliminary efficacy of AFM13 monotherapy in R/R CD30+ lymphoma with cutaneous presentation
- 10 patients treated in 4 dose cohorts

Overview:**

- AFM13 monotherapy is active post-Brentuximab vedotin failure
- Biomarker data: possible correlation between response and tumor NK cell infiltration pre-therapy

Results

Cohort	Disease	Toxicity	Response
1	S-ALCL, Alk (-)	No AE	PR
	T-MF	No AE	POD
	C- ALCL	Rash (G4) Skin infection (G3)	CR
2	MF	IRR (G1)	SD
	T-MF	IRR (G1)	SD
	T-MF	Skin infection (G3) IRR (G1)	Not assessed
3	T-MF	No AE	PR
	S-ALCL, Alk (-)	No AE	PR
	MF	No AE	POD
4	T-MF	No AE	PR

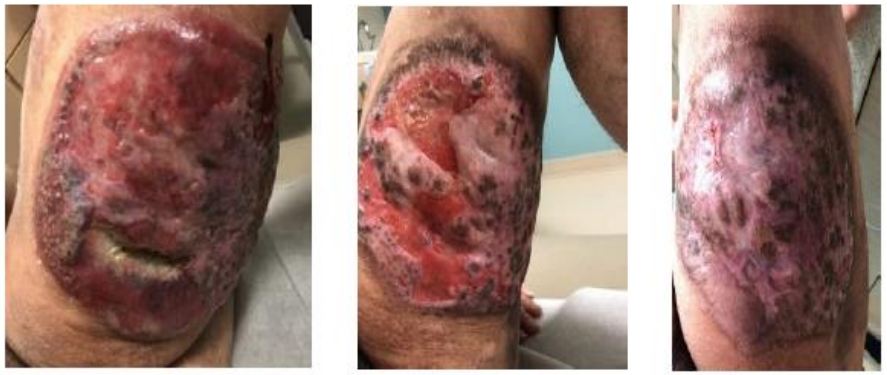
- 50% ORR including 1 CR and 4 PRs

Sawas A et al. ICML 2019

AFM13 monotherapy in patients with CD30+lymphoma

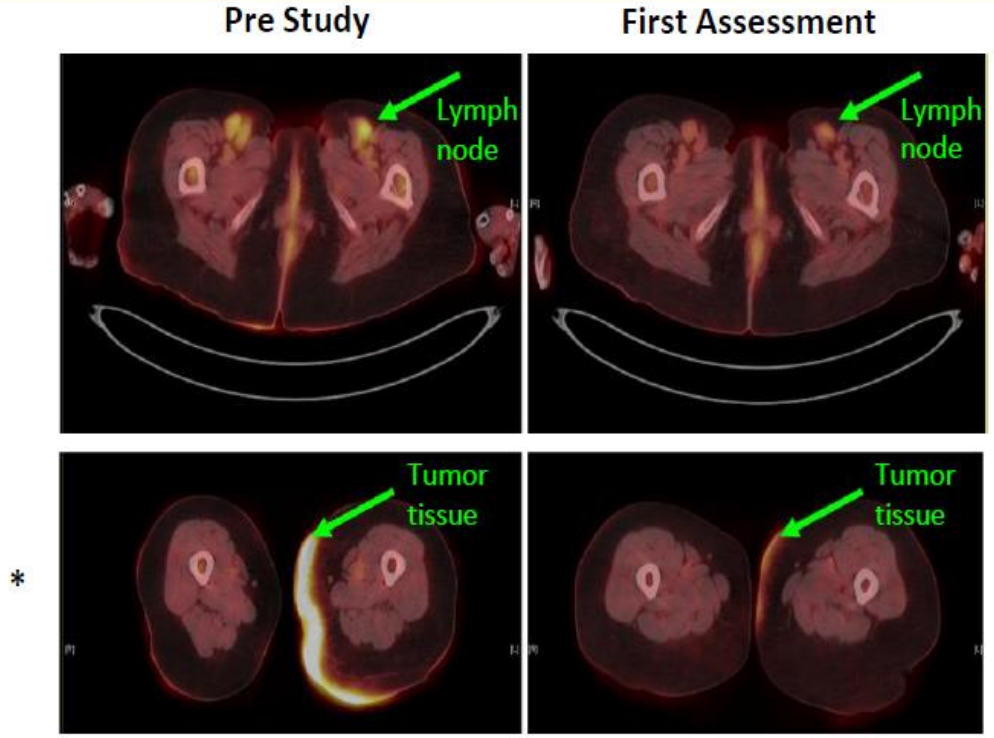
Response: Skin lesions (leg)

Pre Study | Cycle 1 Week 11 | Post Cycle 2



Efficacy in T-MF: Responses were observed in lymph nodes, skin and the peripheral blood

Response: Lymph nodes (PET-CT)



*Imaging response for same leg in left photographs.

Sawas A et al. ICML 2019

AFM 13 for R/R CD30+ PTCL or tMF (REDIRCT)

PRIMARY ENDPOINT:

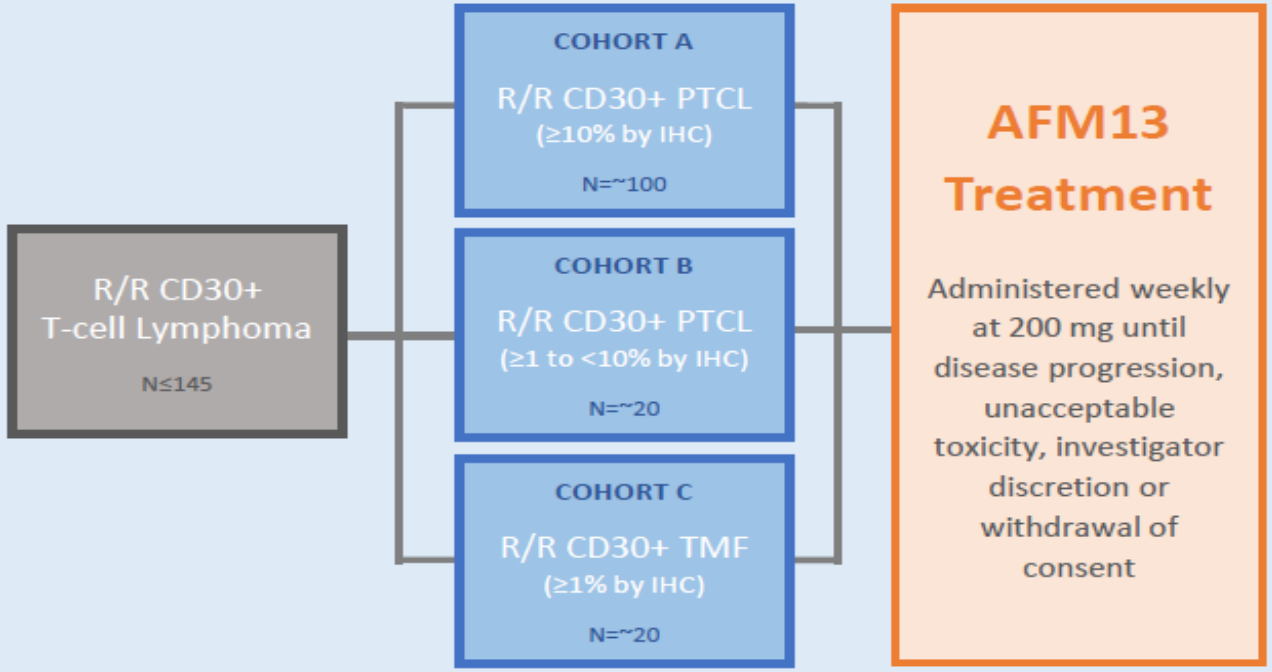
- To assess the antitumor activity of AFM13 by Independent Review Committee-confirmed ORR

SECONDARY ENDPOINTS:

- To assess the antitumor activity of AFM13 by investigator-assessed objective response rate (defined as ORR-2)
- To assess the duration of response (DOR) to AFM13
- To assess the safety and tolerability of AFM13
- To assess the serum pharmacokinetics (PK) of AFM13
- To assess the immunogenicity of AFM13
- To assess quality of life (QoL) of patients while on treatment with AFM13

EXPLORATORY ENDPOINTS:

- Additional exploratory endpoints will be investigated



Hastrick A et al. ASCO 2020

REDIRCT phase 2 trial

INCLUSION CRITERIA OF NOTE:

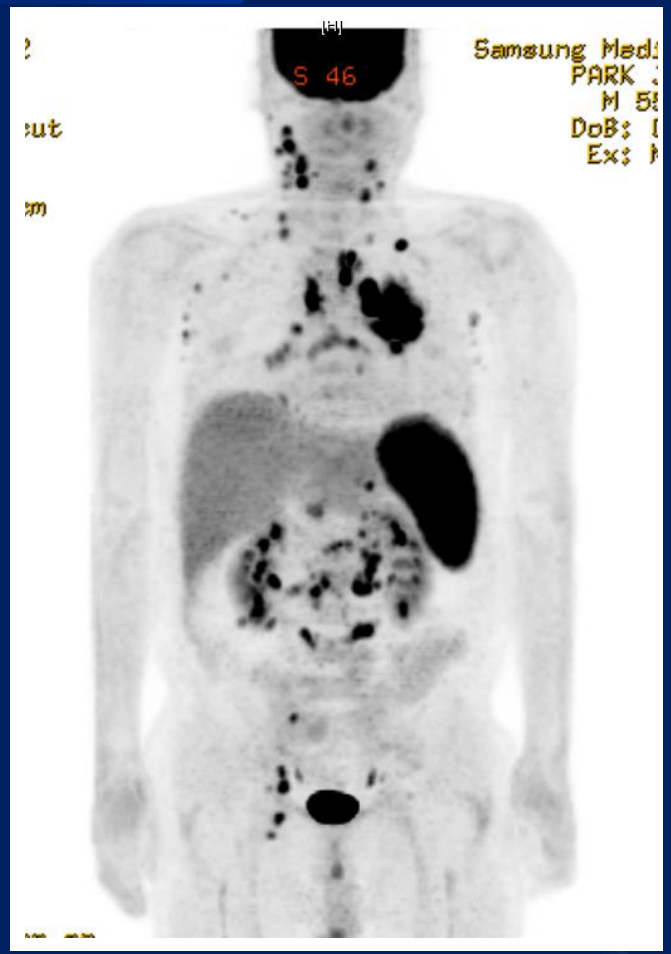
- Eligible patients at least 18 years of age with CD30+ PTCL must have received at least 1 prior line of systemic therapy and, if diagnosed with systemic ALCL, must have failed or be intolerant to brentuximab vedotin (Cohorts A and B)
- Eligible patients at least 18 years of age with CD30+ TMF must have received at least 1 prior line of systemic therapy and have exhausted systemic therapies with regular approval for their disease (Cohort C)
- The PTCL subtypes allowed for cohorts A and B:
  - Enteropathy-associated T-cell lymphoma
  - Monomorphic epitheliotropic intestinal T-cell lymphoma
  - Hepatosplenic T-cell lymphoma
  - Subcutaneous panniculitis-like T-cell lymphoma
  - Peripheral T-cell lymphoma, not otherwise specified (NOS)
  - Angioimmunoblastic T-cell lymphoma
  - Follicular T-cell lymphoma
  - Nodal peripheral T-cell lymphoma with TFH phenotype
  - Anaplastic large-cell lymphoma, anaplastic lymphoma kinase (ALK)-positive
  - Anaplastic large-cell lymphoma, ALK-negative
  - Breast implant-associated anaplastic large-cell lymphoma

EXCLUSION CRITERIA OF NOTE:

- Patients with the following subtypes of lymphoma:
  - T-cell prolymphocytic leukemia
  - T-cell large granular lymphocytic leukemia
  - Chronic lymphoproliferative disorder of NK cells
  - Aggressive NK-cell leukemia
  - Extranodal NK-/T-cell lymphoma
  - Indolent T-cell lymphoproliferative disorder of the gastrointestinal tract
- Current evidence of central nervous system involvement
- Has had an allogenic tissue hematopoietic stem cell/solid organ transplant within the past 3 years. *Note: Patients who have had a transplant >3 years ago are eligible as long as there are no signs/symptoms of graft versus host disease (GvHD)*
- Requirement for systemic immunosuppressive therapy (eg, GvHD therapy, <12 weeks prior to the first dose of study drug)

Hastrick A et al. ASCO 2020

M/55 PTCL, NOS [Cohort A]



Lymph node, cervical, right, "4", excisional biopsy :

EBV-POSITIVE PTCL-NOS

<< Result of immunohistochemistry
. CD3: Positive
. CD 30 : Positive (3+, 50%)e
. Granzyme B:Positive
. Ki-67: About 50-60% .

1) CHOP #2 (19.08.28 - 19.09.18) : PD

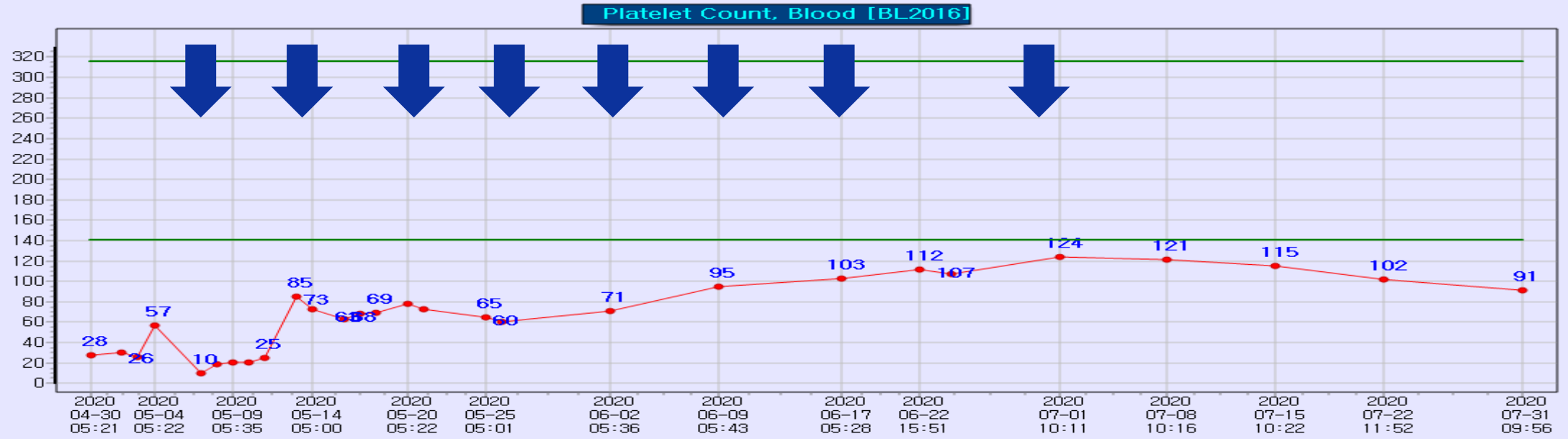
2) ICE/Dexa #4 (19.10.21 - 20.01.18) : PR

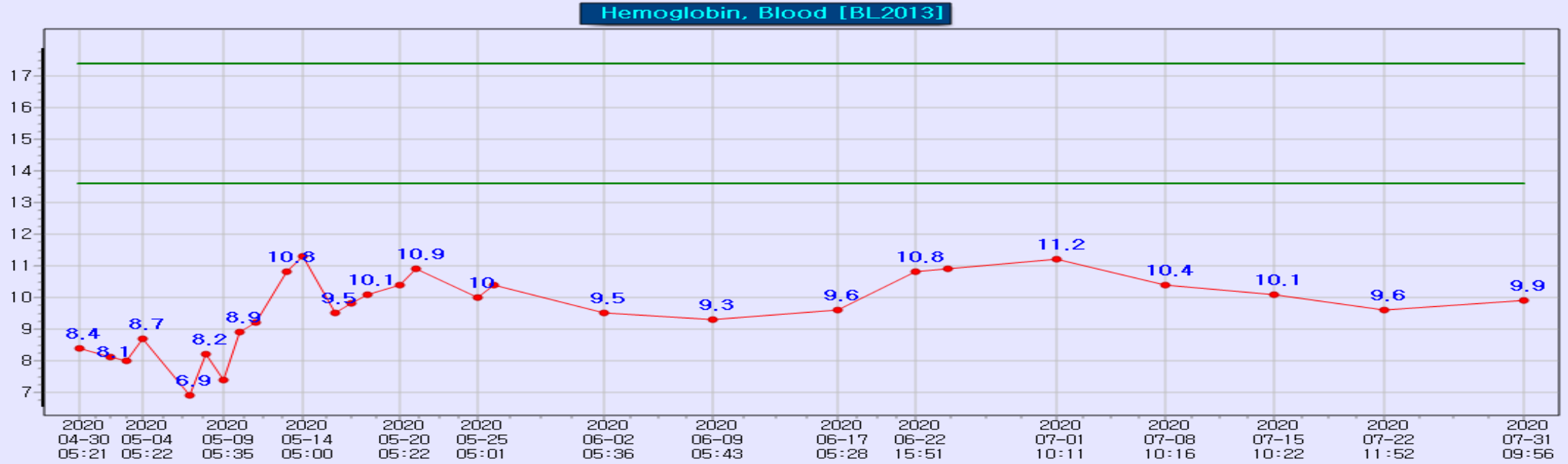
3) etoposide mobilization (20.02.12)

4) 20.02.28 auto-HSCT

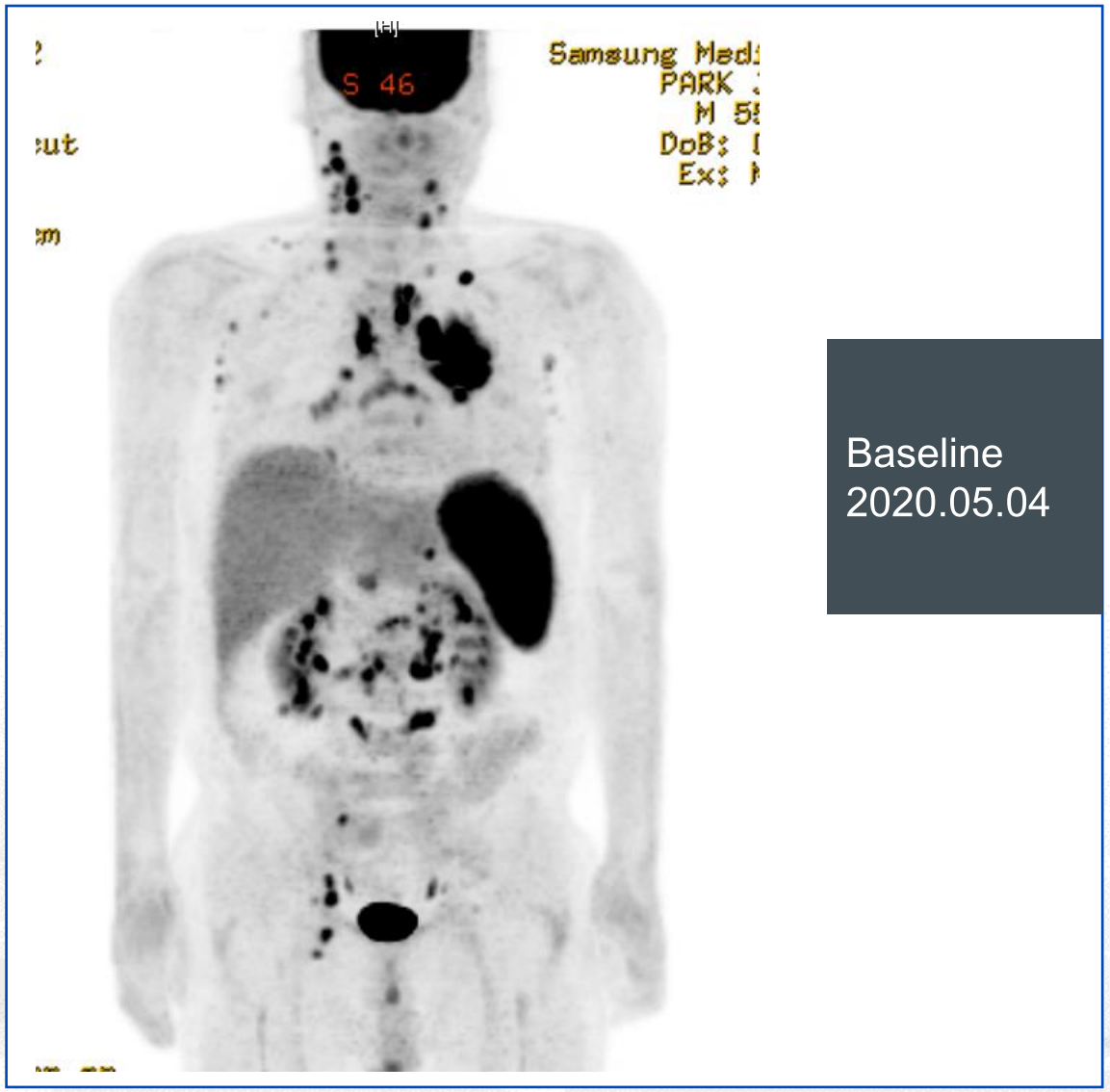
5) 2020.4 fever and cytopenia

Baseline 2020.05.04

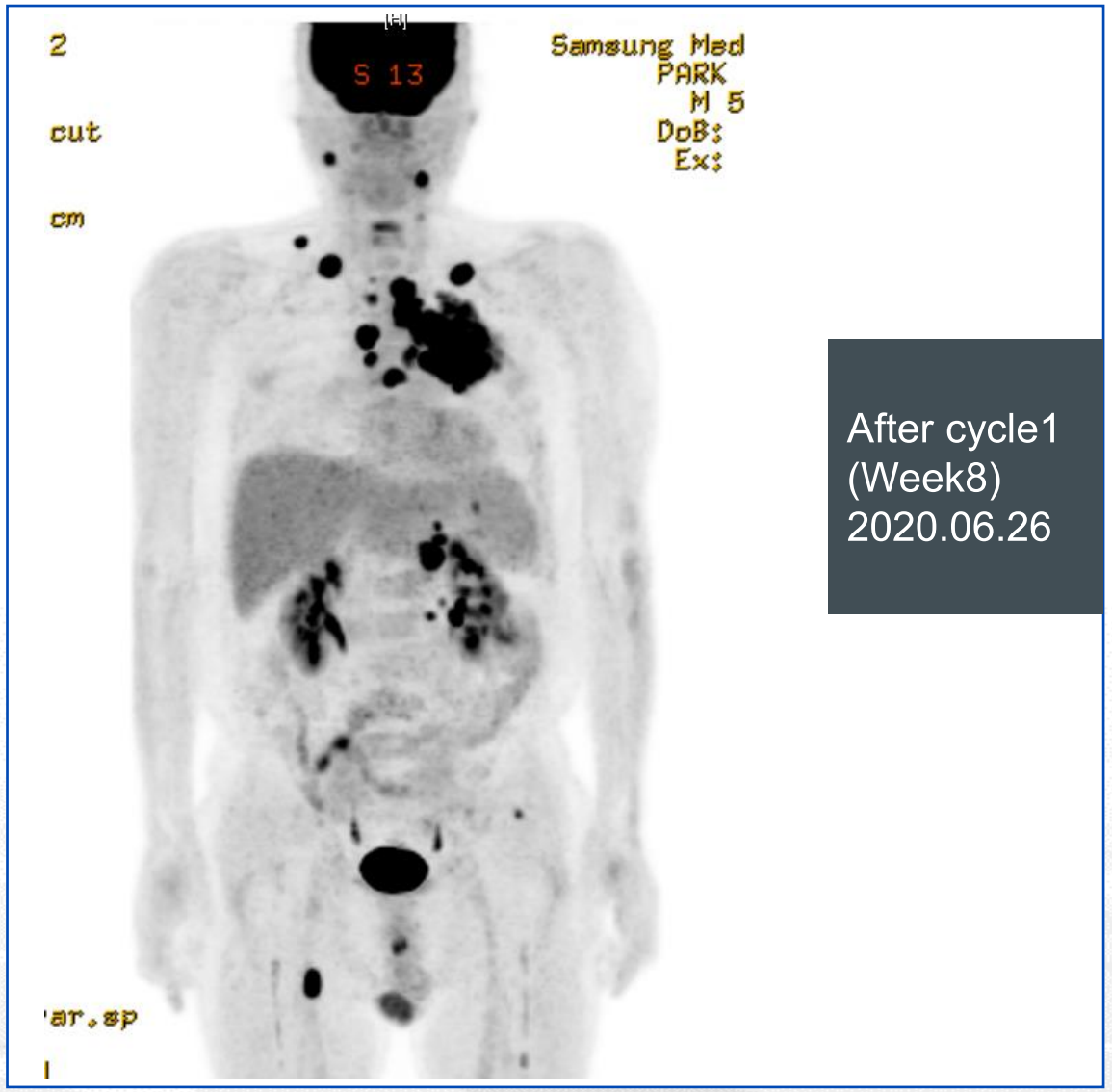

Platelet Count, Blood [BL2016]
320
300
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
28
26
57
10
25
85
73
69
65
60
71
95
103
112
107
124
121
115
102
91
2020 04-30 05:21
2020 05-04 05:22
2020 05-09 05:35
2020 05-14 05:00
2020 05-20 05:22
2020 05-25 05:01
2020 06-02 05:36
2020 06-09 05:43
2020 06-17 05:28
2020 06-22 15:51
2020 07-01 10:11
2020 07-08 10:16
2020 07-15 10:22
2020 07-22 11:52
2020 07-31 09:56


Hemoglobin, Blood [BL2013]
17
16
15
14
13
12
11
10
9
8
7
8.4
8.1
8.7
6.9
8.2
8.9
10.8
9.5
10.1
10.9
10
9.5
9.3
9.6
10.8
11.2
10.4
10.1
9.6
9.9
2020 04-30 05:21
2020 05-04 05:22
2020 05-09 05:35
2020 05-14 05:00
2020 05-20 05:22
2020 05-25 05:01
2020 06-02 05:36
2020 06-09 05:43
2020 06-17 05:28
2020 06-22 15:51
2020 07-01 10:11
2020 07-08 10:16
2020 07-15 10:22
2020 07-22 11:52
2020 07-31 09:56

M/55 PTCL, NOS [Cohort A]

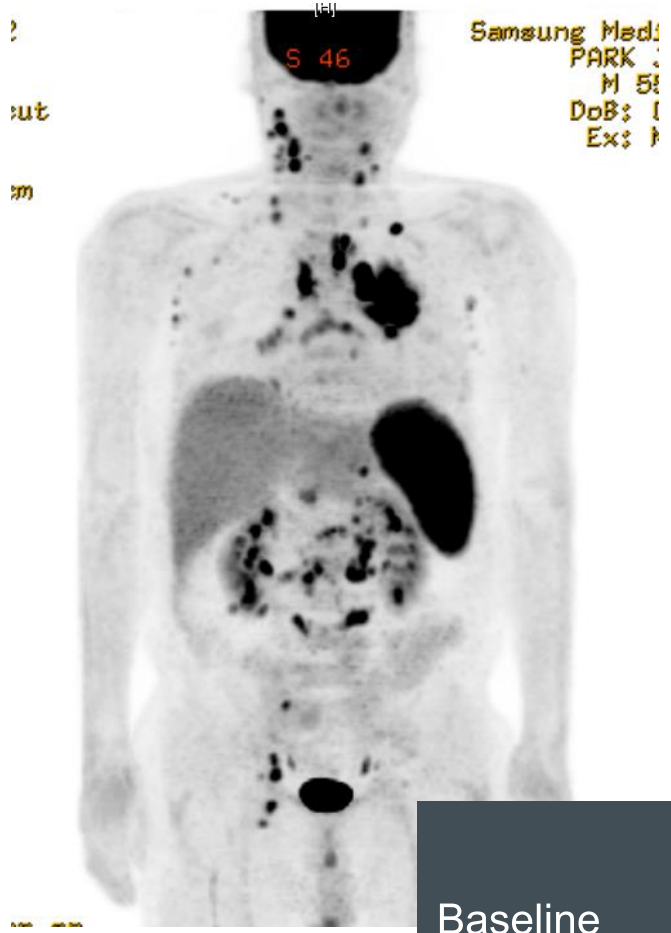


Baseline
2020.05.04

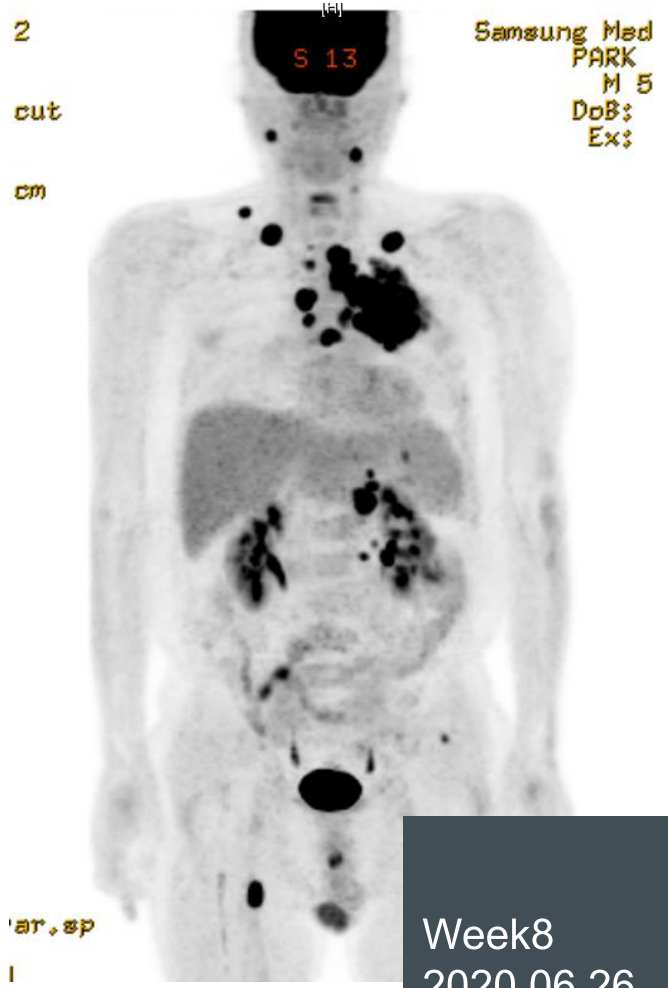


After cycle1
(Week8)
2020.06.26

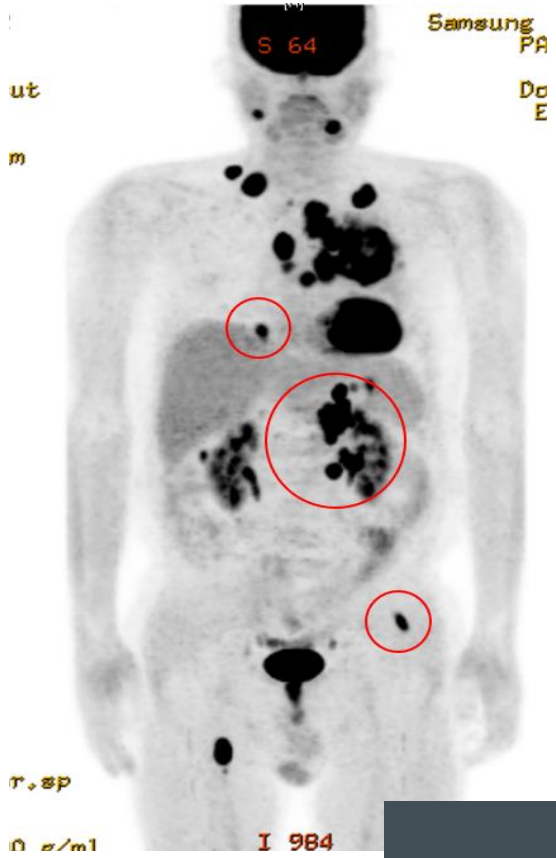
M/55 PTCL, NOS [Cohort A]



Baseline
2020.05.04



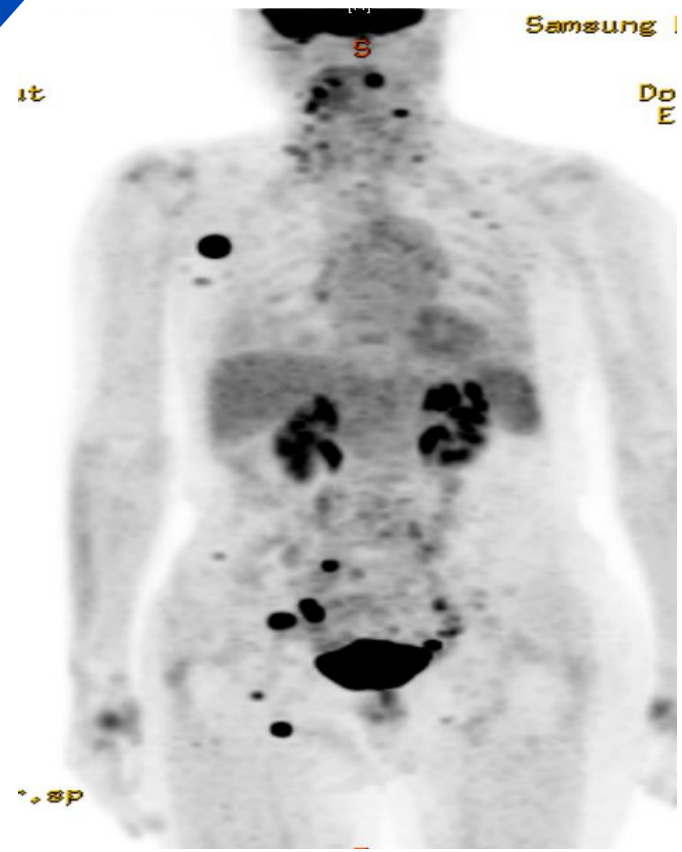
Week8
2020.06.26



CD 30 :
Positive (2+, 90%)
CD 56 :
Weak positive in tumor cells

Week12
2020.07.24

F/68 AITL [Cohort B]



[Diagnosis] AITL (2019.02.14)

[Chemo history]

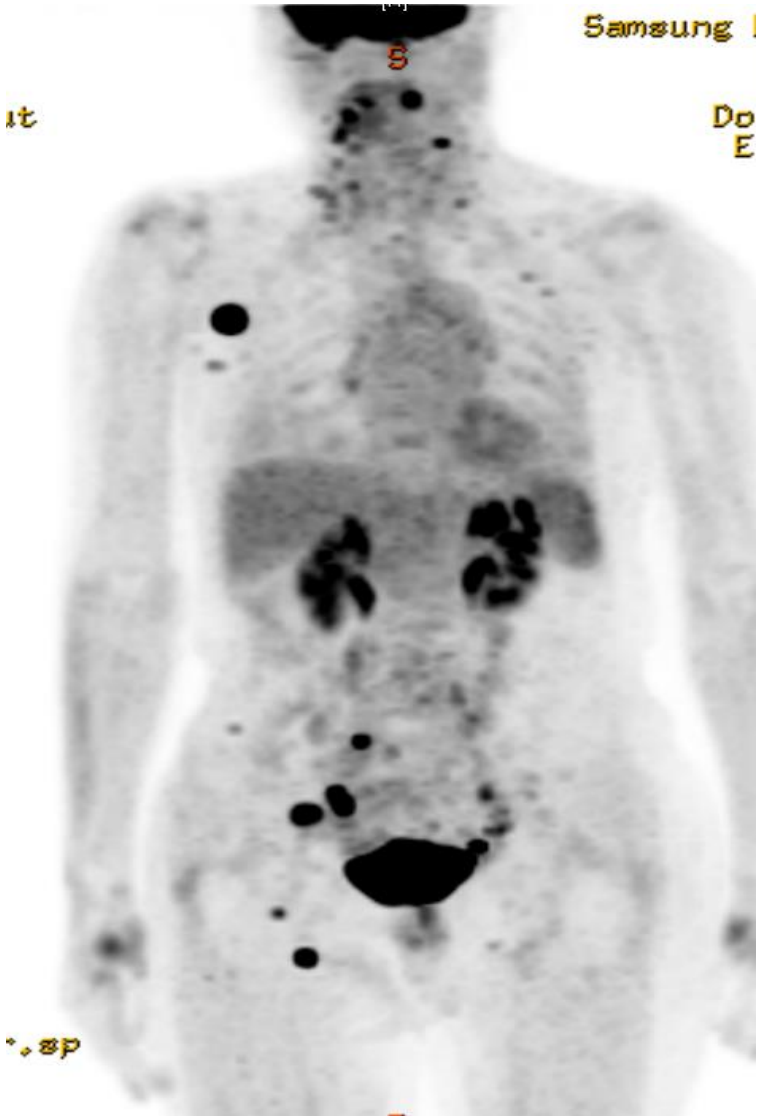
1) EPOCH #6 (2019.02.20 - 2019.06.21) -> CR
2) GDP#4 (2019.11.13-2020.02.14) -> PD

[CD30 IHC] Local: 10% / Central confirm: ≥5% to <10%

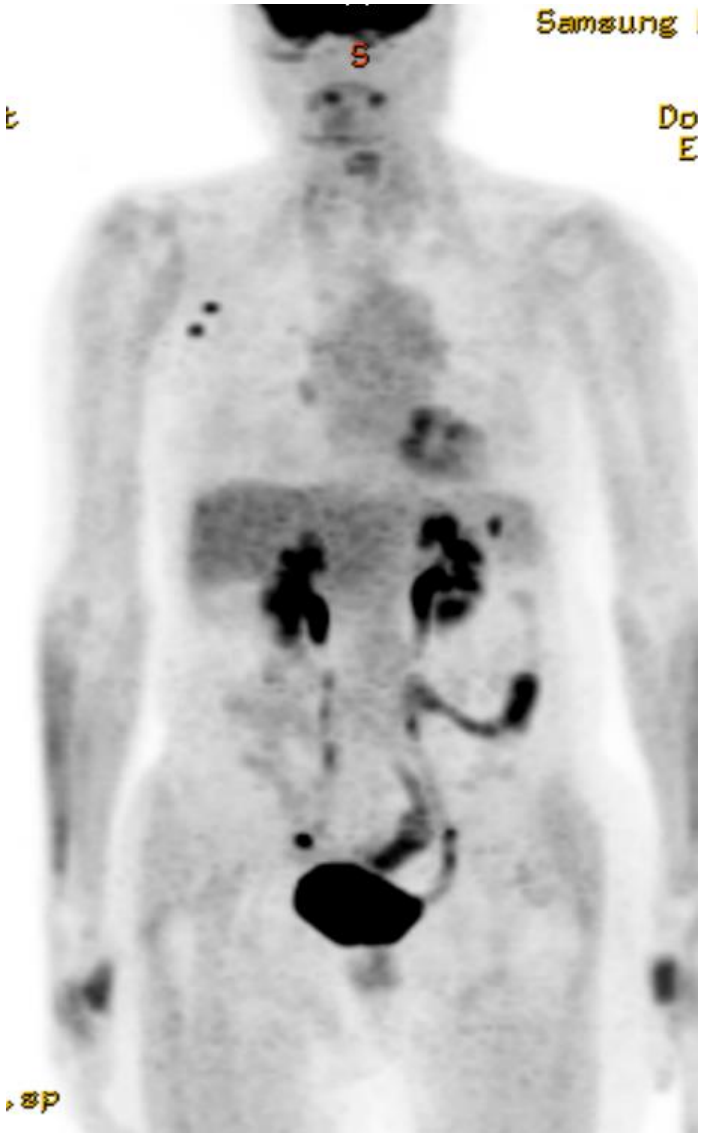
[Schedule]

1) C1D1: 2020.07.06

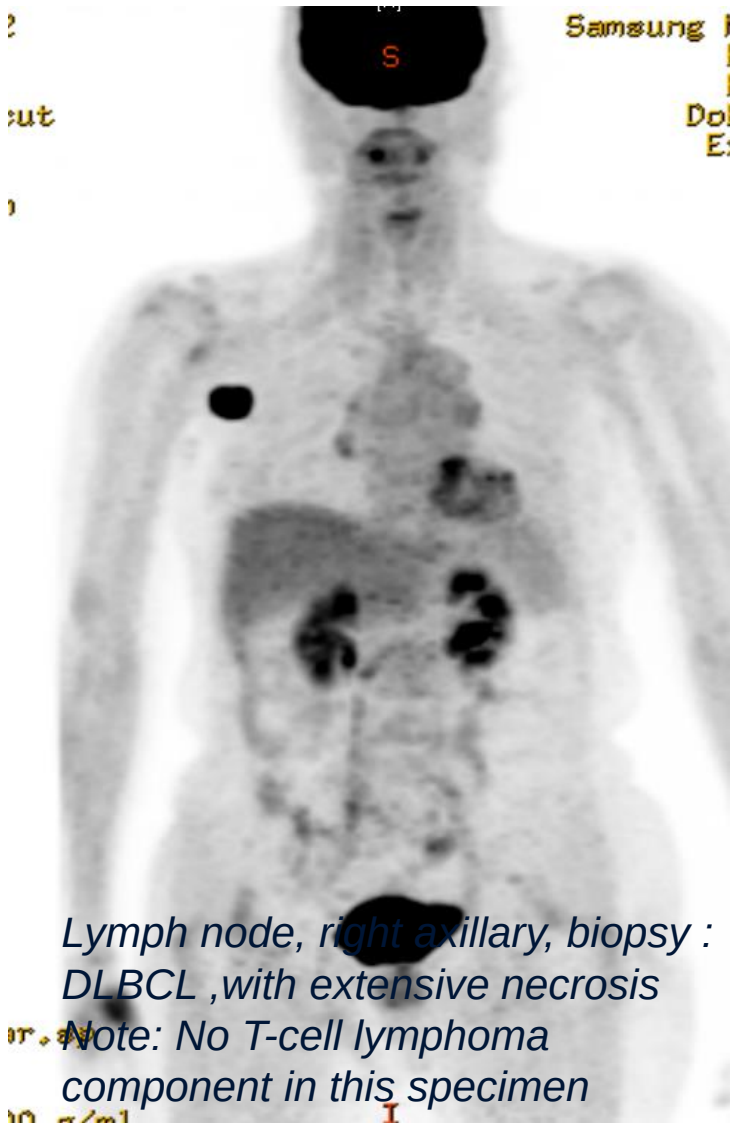
F/68 AITL [Cohort B]



2020.6.13



2020.8.27



Lymph node, right axillary, biopsy : DLBCL ,with extensive necrosis
Note: No T-cell lymphoma component in this specimen

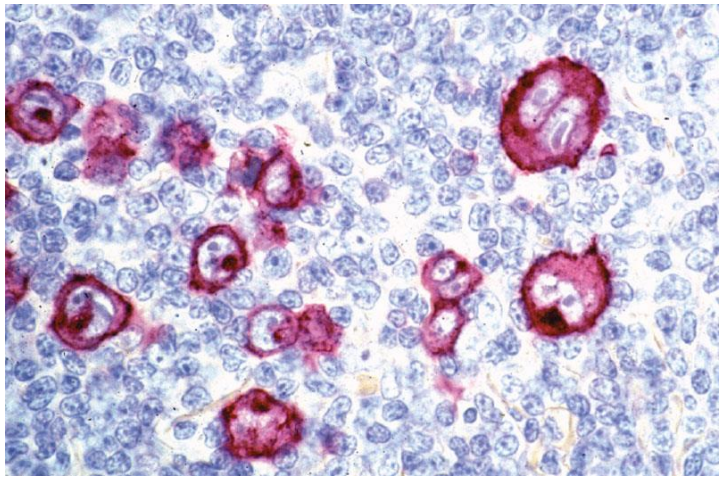
2021.8.23

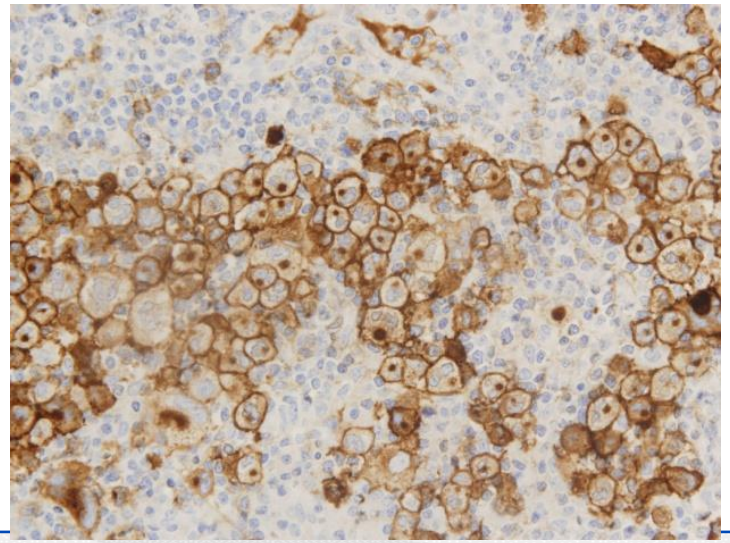
Efficacy and toxicities

Expression in lymphoma subtypes

Classic Hodgkin Lymphoma	**98%**
Nodular LP Hodgkin Lymphoma	<8%
ALCL	**100%**
AITL	0-33%
PTCL-NOS	5-52%
Mycosis fungoides	11-12%
DLBCL	4-25%
Primary Mediastinal LBCL	69-86%
Follicular lymphoma	14-50%
Burkitt lymphoma	18%
Adult T-cell leukemia/lymphoma	0-33%
Enteropathy-associated T-cell Lymphoma	38-100%
Extranodal NK/T-cell lymphoma	14-50%

CD30 Expression is heterogeneous in non-Hodgkin lymphoma





CD30 expression in peripheral T cell lymphomas

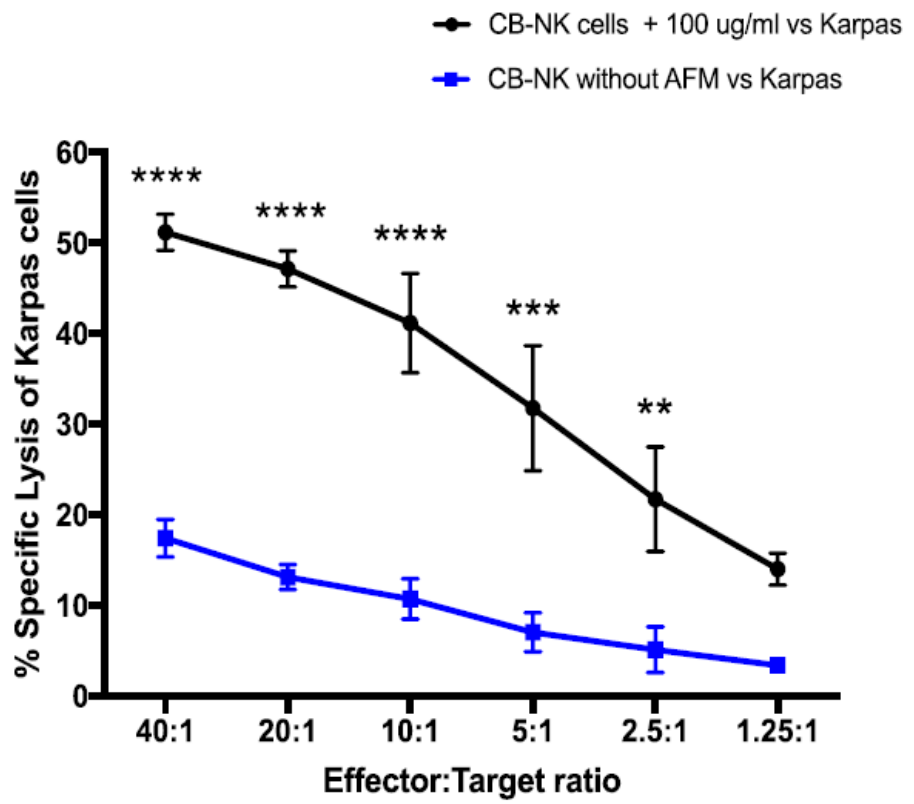
% of CD30$^+$ tumor cells	ALCL ALK$^+$ (N = 61)	ALCL ALK$^-$ (N = 19)	PTCL NOS (N = 141)	AITL (N = 97)	ENKTL (N = 28)	EATL (N = 14)	ATLL (N = 9)	HSTL (N = 7)
Score 0	0	0	59	36	15	7	4	7
<5%			42%	37%	53.5%	50%	44%	100%
Score 1	0	0	37	46	2	0	1	0
5-24%			26%	47%	7%		11%	
Score 2	3	0	13	10	3	0	3	0
25-49%	5%		9%	10%	11%		33%	
Score 3	1	0	14	5	4	1	1	0
50-75%	2%		10%	5%	14%	7%	11%	
Score 4	57	19	18	0	4	6	0	0
>75%	93%	100%	13%		14%	43%		
Total positive cases (scores 1-4)	61	19	82	61	13	7	5	0
	100%	100%	58%	63%	46%	50%	55.5%	
Strongly positive cases (scores 3-4)	58	19	32	5	8	7	1	0
	95.1%	100%	23%	5%	28.5%	50%	11%	

ENKTL, extranodal natural killer/T-cell lymphoma; HSTL, hepatosplenic T-cell lymphoma.

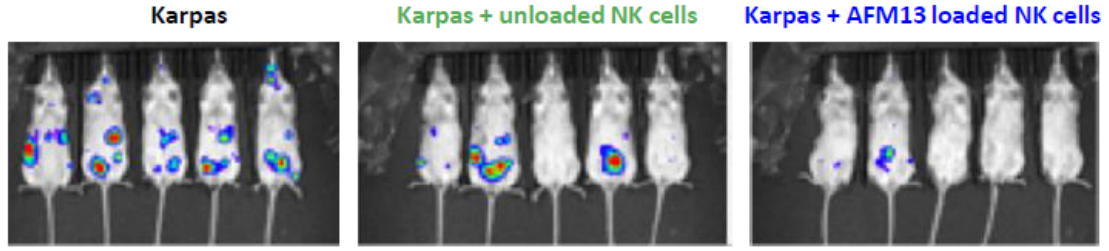
Bossard C. et al. Blood 2014;124:2983

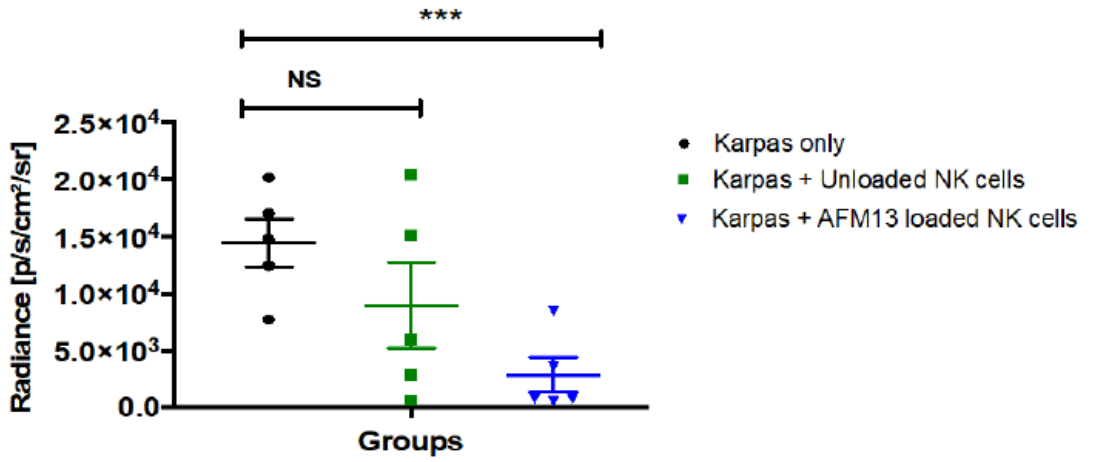
AFM13 and Cord blood derived NK cell

AFM13-loaded cbNK cells kill CD30+ cells *in vitro*



AFM13-loaded cbNK cells demonstrated reduction in tumor volume *in vivo* (Day 21)





Kerbauy et al. ASH 2018

Conclusion

The efficacy of AFM13 in PTCL is confirmed with minimal toxicities.

Based on the preclinical model, combination of NK-cell seems to be promising.

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THANK-YOU