KB004, a Novel Non-Fucosylated Humaneered® Antibody, Targeting EphA3, is Active and Well Tolerated in a Phase 1/2 Study of Advanced Hematologic Malignancies

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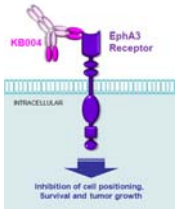
Background



EphA3

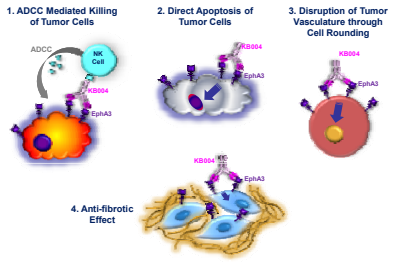
- Novel drug target
- Important in fetal development for cell positioning, but not required in adults
- Oncofetal antigen, not expressed on normal blood or bone marrow cells
- Re-expressed in hematologic malignancies (blood, bone marrow, leukemic stem cells) and solid tumors
- Upregulated in fibrotic diseases (e.g. IPF, diabetic kidney disease)

KB004

- Humaneered® high affinity antibody targeting EphA3 (KD = 610 pM)

Mechanisms of Action

KB004 has 4 Postulated Mechanisms of Action (MOA)

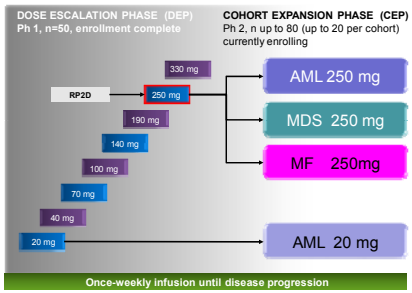


Study Objectives

First-In-Human Study Objectives:

- **Primary:** To determine safety and MTD of KB004 in patients with hematologic malignancies, refractory to or ineligible for chemotherapy
- **Secondary:** To characterize PK, immunogenicity, and preliminary clinical activity of KB004
- **Exploratory:** To evaluate EphA3 expression on tumor, stromal, and endothelial cells

KB004-01 Phase 1/2 Study Design and RP2D



Rationale for Selection of 250 mg Dose Level as RP2D:

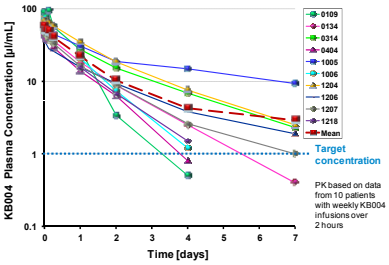
- **PK:** Sustained KB004 plasma exposure above predicted effective plasma concentration (1 µg/mL) achieved at 250 mg
- **Safety**: At 330 mg, one patient had a Grade 3 infusion related reaction (DLT) and a second patient required multiple dose interruptions. A maximum tolerated dose (MTD) was not reached

Rationale for 20 mg Dose Level:

CRi observed, Plasma concentration of 1-10 µg/mL achieved; excess antibody could interfere with EphA3 activation, efficient cross-linking needed for endothelial cell-rounding MOA

RP2D KB004 Plasma Concentration

Mean KB004 plasma concentration for 250 mg dose group is at or above a target level of 1µg/mL at 7 days post dosing



PK based on data from 10 patients with weekly KB004 infusions over 2 hours

Baseline Demographics

Baseline Demographics[1]	AML (n=47)	MDS (n=4)	MDS/MPN (n=4)	MF[2] (n=1)	Other (n=2)	Total (n=58)
Age [Years]						
Median Age [min, max]	70.0 [25, 89]	70.5 [68, 80]	77.0 [67, 84]	73.00 [73, 73]	58.0 [50, 66]	**70.0 [25, 89]**
Sex [n(%)]						
Male	29 (61.7)	2 (50.0)	3 (75.0)	1 (100.0)	2 (100.0)	**37 (63.8)**
Female	18 (38.3)	2 (50.0)	1 (25.0)	-	-	**21 (36.2)**
Race [n(%)]						
Asian	2 (4.3)	-	-	-	-	**2 (3.4)**
Black/African American	3 (6.4)	-	-	-	-	**3 (5.2)**
White	42 (89.4)	4 (100.0)	3 (75.0)	1 (100.0)	2 (100.0)	**52 (89.7)**
Other	-	-	1 (25.0)	-	-	**1 (1.7)**
ECOG Status [n(%)]						
0	21 (44.7)	2 (50.0)	3 (75.0)	-	1 (50.0)	**27 (46.6)**
1	26 (55.3)	2 (50.0)	1 (25.0)	1 (100.0)	1 (50.0)	**31 (53.4)**
EphA3 Status[3,4] [n(%)]						
EphA3 positive	26 (72.2)	3 (75.0)	2 (50.0)	1 (100.0)	2 (100.0)	**34 (73.9)**
EphA3 negative	2 (5.6)	-	1 (25.0)	-	-	**3 (6.5)**
Prior Regimens [n(%)]						
2 or less, [min, max]	6 (15.4) [0, 2]	3 (75.0) [1, 2]	4 (100.0) [0, 2]	-	-	**12 (24.0) [0,2]**
3 or more, [min, max]	31 (79.5) [3, 8]	1 (25.0) [3]	-	1 (100.0) [3]	2 (100.0) [3]	**34 (68.0) [3,8]**

[1] Includes 50 DEP and 8 CEP patients
[2] Total of 3 MF patients:1 MF patient is included with 'MDS/MPN' and one with 'Other'
[3] Patients with evaluable bone marrow samples only (19.6% not evaluable). EphA3 positivity was not an inclusion criteria for DEP. EphA3 positivity is required for CEP
[4] EphA3 positivity defined as more than 10% of nucleated cells by IHC

Adverse Events Regardless of Reported Causality

KB004-01 treatment emergent adverse events occurring in at least 10% of patients

MedDRA Preferred Term, n (%)	Toxicity by Severity, n=58 (50 DEP + 8 CEP patients) Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Total
Infusion Related Reaction*	6 (10.3)	37 (63.8)	2 (3.4)	-	-	**45 (77.6)**
Febrile Neutropenia	-	-	15 (25.9)	-	-	**15 (25.9)**
Anaemia	-	2 (3.4)	10 (17.2)	-	-	**12 (20.7)**
Pneumonia	-	-	8 (13.8)	-	2 (3.4)	**10 (17.2)**
Pyrexia	4 (6.9)	6 (10.3)	-	-	-	**10 (17.2)**
Decreased Appetite	3 (5.2)	4 (6.9)	-	-	-	**7 (12.1)**
Hyperglycaemia	2 (3.4)	-	5 (8.6)	-	-	**7 (12.1)**
Fatigue	1 (1.7)	4 (6.9)	2 (3.4)	-	-	**7 (12.1)**
Nausea	2 (3.4)	4 (6.9)	1 (1.7)	-	-	**7 (12.1)**
Diarrhoea	5 (8.6)	2 (3.4)	-	-	-	**7 (12.1)**
Thrombocytopenia	-	-	3 (5.2)	3 (5.2)	-	**6 (10.4)**
Back Pain	4 (6.9)	1 (1.7)	1 (1.7)	-	-	**6 (10.3)**
Constipation	6 (10.3)	-	-	-	-	**6 (10.3)**

* Only adverse event in this list deemed (by KaloBios) to be related to KB004 administration

Serious Adverse Events (SAEs) Reported

- **44 of 58 (75.9%) patients experienced SAEs**: various infections (41.4% of patients), febrile neutropenia (20.7% of patients), infusion related reactions (13.8% of patients)
- **SAEs deemed by KaloBios, to be at least possibly related to KB004 administration were experienced by 10 patients:** Infusion related reactions (8 patients), intracranial hemorrhage* (2 patients)

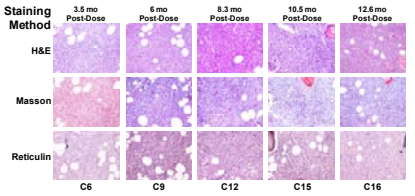
* Both patients had concomitant progressive disease (late stage AML) and significant thrombocytopenia. Two Independent reviews of KB004 soluble clotting factors were conducted – no data suggested a KB004-related adverse effect on the soluble phase coagulation system. The two reports occurred under an earlier version of the protocol. Enrollment criteria have been updated and no further cases were reported

IWG Responses

Patient #	102-0121	112-1201	112-1206
Age and Sex	78 yr old male	67 yr old male	84 yr old male
Diagnosis	**relapsed AML, prior MDS**	**Myelofibrosis (with anemia)**	**intermediate risk MDS/MPN overlap disease**
EphA3 status at screening	30% positive, SHS[a] score 90	40% positive, SHS[a] score 80	20% positive, SHS[a] score 40
Dose Level	20 mg	140 mg	250 mg
IWG Response	CRi[b]	CI[c]	HI-E[c]
Response Details (Cycle)	• Cycle 5 (3.5 mo): Extensive stromal damage, collagen and reticulin fibrosis at baseline resolved • Cycle 11 (7.7 mo): BMBx showed normal megakaryocyte numbers (previously absent or markedly reduced)	• Evidence of improvement with a decrease in spleen size, improvement in collagen fibrosis. • Transfusion independent since Cycle 7 (4.9 mo) up to Cycle 19 (13.3 mo)	• Improved hemoglobin count in Cycle 12 (8.4 mo)
Study status	• Patient withdrawn in Cycle 27 (18.9 mo) due to progressive disease	• Patient off study after Cycle 19 (13.3 mo) due to renal failure/infection	• Ongoing in Cycle 18 (12.6 mo)

[a] SHS calculated by multiplying % of nucleated cells positive for EphA3 expression by the staining intensity (scale of 0 to 3)
[b] by 2003 IWG Criteria (Cheson, 2003); [c] by 2006 IWG Criteria (Cheson, 2006)

Marrow Recovery & Improved Fibrosis in MF Patient



Photograph panel showing the fibrosis status for several biopsies for MF patient 112-1201. Report from hematopathologist German Campuzano-Zuluaga, University of Miami, FL: *"There is marked improvement of fibrosis towards the end of the series"*

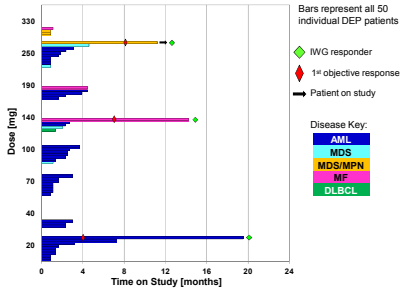
≥ 50% BM Blast Reduction and EphA3 Expression

Cohort	Disease	Patient #	Baseline Bone Marrow Blasts [%]	Minimum Post-Baseline Bone Marrow Blasts [%]	EphA3 Simplified H Score[a] (SHS, 0-300) at Baseline Determined by IHC
20 mg	**AML**	**102-0121[a]**	**5[b]**	**2**	**90**
100 mg	AML	102-0128	60	26	6
140 mg	MDS	111-1101	28	10	ND
140 mg	**MF**	**112-1201[a]**	**5**	**2**	**80**
190 mg	AML	102-0132	29	10	80
190 mg	AML	105-0506	16	4	60
190 mg	MF	103-0311	7	3	10
250 mg	MDS	112-1207	2	1	60
250 mg	**MDS/MPN**	**112-1206[a]**	**4**	**1**	**40**

ND= no data

IWG responder [b] Hemodilute aspirate, blasts 2-34% on biopsy
[c] SHS calculated by multiplying % of nucleated cells positive for EphA3 expression by the staining intensity (scale of 0 to 3)

IWG Responses Observed After 4 Months



Conclusions

- KB004 is a Humaneered® high affinity antibody against the novel drug target EphA3
- Phase 1 (DEP) data shows KB004 is well tolerated and has promising clinical activity
- The recommended Phase 2 dose was determined as 250 mg; MTD was not reached
- Phase 2 (CEP) is ongoing, where KB004 activity will be characterized at 250 mg in disease specific cohorts (AML, MDS and MF)
- CEP inclusion criteria include EphA3 positivity and no more than 2 prior therapies for AML patients

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Disclaimers

Data presented from this ongoing study are preliminary and subject to change.

Disclosures:
Durrant: KaloBios: Research Funding, Yarranton: KaloBios: Employment, Equity Ownership;Glaxo: Equity Ownership; EnGen: Equity Ownership, Science Advisor, Science Advisor Other; StemLine Therapeutics: Equity Ownership. Krupka: KaloBios Employment; Walling: KaloBios: Consultancy; Corcept Therapeutics: Consultancy; Prothena: Consultancy; New Gen Therapeutics: Consultancy; Valent Technologies: Consultancy; LBC Pharmaceuticals: Consultancy; Amgen: Equity Ownership; BioMarin: Equity Ownership; Crown BioScience: Membership on an entity's Board of Directors or advisory committees