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ABSTRACT #2575

Inhaled KB707, a Novel HSV-based Immunotherapy, as a Monotherapy in Patients with Advanced Solid Tumor Malignancies Affecting the Lungs: Efficacy and Safety Results from a Phase 1/2 Study

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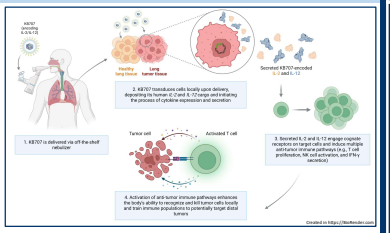
BACKGROUND

Clinical use of recombinant interleukin (IL)-12 and IL-2 has been hindered due to unfavorable kinetics and toxicity associated with systemic exposure. Patients with advanced non-small cell lung cancer (NSCLC) who do not respond to immune checkpoint inhibitors (ICI) have very limited therapeutic options.

KB707, a replication-defective herpes simplex virus type 1 (HSV-1)-based vector encoding human IL-12 and IL-2, is a novel gene therapy designed to deliver high doses of cytokines to the local tumor microenvironment.

This study evaluated whether KB707 administered by inhalation, would deliver efficacious dose to the lung while minimizing systemic exposure in advanced solid tumor patients with predominantly lung disease.



CONCLUSIONS

- **Inhaled** delivery of KB707 was **safe** and **well tolerated** with most adverse events being Grade 1 or 2 and transient in duration. The MTD was not reached and recommended phase 2 dose is 10^9 PFU.
- **Single agent KB707** demonstrated **anti-tumor effects** in heavily pre-treated NSCLC patients with **ORR of 27%.** In the extended follow-up after the data cut, an additional patient achieved partial response for an **updated ORR of 36%. Response was durable with median DOR and PFS not reached.**
- The delivery of cytokines via our **novel vector platform** suggests that KB707 may have a synergistic effect with immune checkpoint inhibitors to enhance anti-tumor activity and potentially overcoming primary anti-PD1 resistance. The promising combination of KB707 with anti-PD-1 is currently under evaluation in the expansion cohorts with ongoing enrollment of patients to receive inhaled KB707 in combination with pembrolizumab.

METHODS

NCT06228326 is a Phase 1/2, open-label, dose escalation and expansion clinical trial of inhaled KB707

- **Monotherapy:** Enrolled patients had at least one measurable lung lesion at screening and histological confirmation of advanced solid tumor malignancy in the lungs.
- **Combination Therapy:** Enrolling patients with histologically or cytologically confirmed diagnosis of stage 3 or 4 non-small cell lung cancer (NSCLC)
- **Assessments**: Safety, immunologic biomarkers, and preliminary efficacy.

ABSTRACT DATA PRESENTED[1]
Monotherapy (Enrollment Complete)

Solid Tumors Malignancy (Cohorts 1-4)

Dose Escalation (n=16) 10^8 to 10^9 PFU → *Dose Selected* → Dose Expansion (n=23) 10^9 PFU

KB707 Monotherapy Dosing Schematic

[1] Efficacy data presented in indication with substantial number of subjects enrolled who had at least one efficacy evaluation per RECIST v1.1

Combination Therapy (Enrolling[1])

Advanced NSCLC (Cohorts 5 and 6)

KB707 + Keytruda | KB707 + Keytruda + Chemotherapy

[1] Eligible patients may rollover from monotherapy cohorts 1-4

ENROLLMENT & DISPOSITION

Safety population (n=39) consists of subjects who received at least one dose of inhaled KB707 as monotherapy. Tumor types evaluated included: NSCLC, head and neck cancer, breast cancer, colorectal cancer, and other cancer types

Efficacy population (n=11) consists of subjects with NSCLC, the indication with the largest number of enrolled subjects who had at least one efficacy evaluation per RECIST v1.1.

DEMOGRAPHICS		
Population Tumor Type	**Safety (n=39) Solid Tumors**	**Efficacy (n=11) NSCLC**
Median Age, years (range)	64 (20-80)	71 (54-77)
Gender, n (%)		
Female	24 (61.5)	7 (63.6)
Male	15 (38.5)	4 (36.4)
BASELINE CHARACTERISTICS		
Efficacy-Evaluable NSCLC Subjects (n=11)		
Baseline ECOG Status, n (%)		
0		1 (9.1)
1		10 (90.9)
Disease Stage IV, n (%)		11 (100)
PD-L1 Status, n (%)		
Positive (PD-L1 ≥1%)		2 (18.2)
Negative (PD-L1 <1%)		5 (45.5)
Unknown		4 (36.4)
Prior Therapy		
Median lines		4
1 line of prior immunotherapy, n (%)		7 (63.6)
≥2 lines of prior immunotherapy, n (%)		4 (36.4)

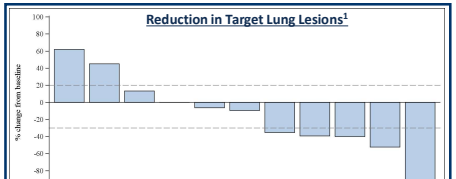
RESULTS

Best Overall Response to Inhaled KB707

Efficacy-Evaluable[1] NSCLC Patients (n=11)		
	Abstract Data Cut	Extended Follow-up[2]
Partial Response (PR)	3	4
Stable Disease (SD)	5	2
Progressive Disease (PD)	3	5
ORR	27%	36%

[1] Patients with at least one post-baseline scan available for RECIST v1.1 response assessment per Investigator
[2] Extended follow-up data snapshot taken 15APR2025.

Reduction in Target Lung Lesions[1]

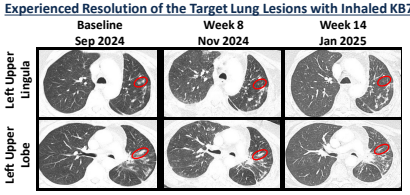


[1] Data includes extended follow-up 15APR2025

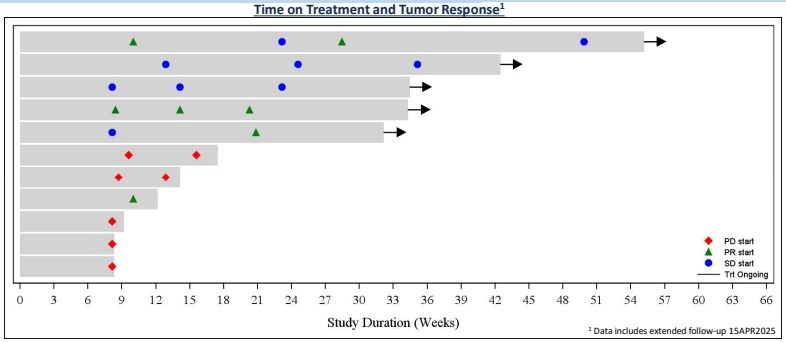
BOR	PD	PD	PD	PD	SD	SD	PR	PR	PD	PR	PR

- Extrapulmonary target lesions were either stable or had progressed

72-year-old with Stage 4 NSCLC (2 lines of prior ICI) Exhibiting Ongoing PR Experienced Resolution of the Target Lung Lesions with Inhaled KB707



Time on Treatment and Tumor Response[1]



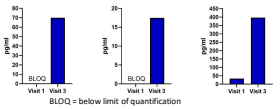
[1] Data includes extended follow-up 15APR2025

Inhaled KB707 Monotherapy is Safe and Well Tolerated

- Most TRAEs were Grade 1 or 2 and transient in duration.
- No Grade 4 or Grade 5 TRAEs
- Patients experiencing ≥1 TRAE = 66.7% (26)

TRAE ≥10% Total Subjects in Safety Population (n=39)				
	Grade 1	Grade 2	Grade 3	Any n(%)
Chills	7 (17.9)	3 (7.7)	0 (0.0)	10 (25.6)
Cytokine Release Syndrome	4 (10.3)	4 (10.3)	1 (2.6)	9 (23.1)
Fatigue	6 (15.4)	2 (5.1)	0 (0.0)	8 (20.5)
Influenza-like Illness	5 (12.8)	1 (2.6)	0 (0.0)	6 (15.4)
Dyspnea	2 (5.1)	3 (7.7)	1 (2.6)	6 (15.4)
Vomiting	3 (7.7)	1 (2.6)	1 (2.6)	5 (12.8)
Pyrexia	3 (7.7)	0 (0.0)	1 (2.6)	4 (10.3)

Early increase in IFN-γ observed after a single dose of inhaled KB707



BLOQ = below limit of quantification

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