ASCO 2026
Annual Meeting
ABSTRACT #8564

Inhaled Delivery of KB707, a Novel HSV-based Immunotherapy, in Combination with Pembrolizumab in Advanced Non-small Cell Lung Cancer: A Phase 1/2 Study

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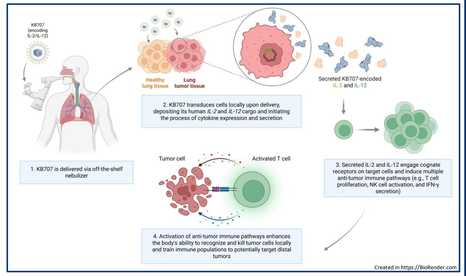
BACKGROUND

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.

KB707 administered by inhalation has been evaluated as monotherapy treatment. Inhaled delivery of KB707 was safe and well tolerated with most adverse events being Grade 1 or 2 and transient in duration. Single agent KB707 demonstrated anti-tumor effects in heavily pre-treated NSCLC patients (Ma WW et al., J Clin Oncol. 2025;43 (16_suppl):2575).

The study has also evaluated whether inhaled KB707 administered in combination with pembrolizumab would have synergistic effect and enhance anti-tumor activity while minimizing systemic exposure in patients with advanced NSCLC.



CONCLUSIONS

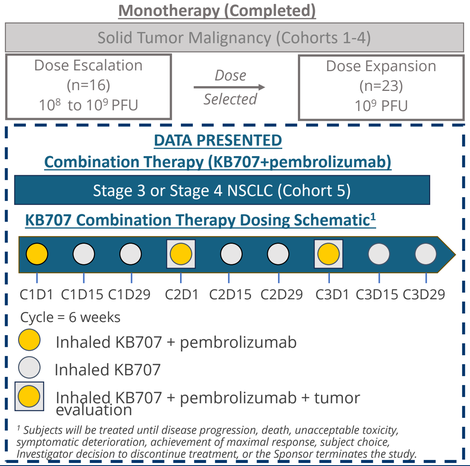
- **Inhaled delivery** of KB707 in combination with pembrolizumab was **safe** and **well tolerated** with most adverse events being Grade 1 or 2 and transient in duration.
- **Combination therapy with inhaled KB707 and pembrolizumab demonstrated anti-tumor effects in advanced NSCLC patients with ORR of 31%. Response was durable with median DOR and PFS not reached.**
- The delivery of cytokines via our **novel vector platform** in combination with pembrolizumab suggests that KB707 may have a synergistic effect with immune checkpoint inhibitors to enhance anti-tumor activity and potentially overcome primary anti-PD1 resistance. Additional combination of KB707 with standard of care is currently under evaluation in the expansion cohorts with ongoing enrollment.

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)
  - Cohort 5: KB707 + pembrolizumab
  - Cohort 6: KB707 + pembrolizumab + chemotherapy
  - Cohort 7: KB707 + docetaxel
- **Assessments**: Safety, immunologic biomarkers, and preliminary efficacy.

Data presented are as of snapshot on 17APR2026.



ENROLLMENT & DISPOSITION

Safety population (n=21) consists of subjects who received at least one dose of inhaled KB707 in combination with pembrolizumab.
Efficacy population (n=16) consists of subjects with NSCLC who received a minimum of 1 treatment cycle and had at least one efficacy evaluation per RECIST v1.1.

DEMOGRAPHICS		
Population	**Safety (n=21)**	**Efficacy (n=16)**
Median Age, years (range)	72 (49-89)	72 (50-88)
Gender, n (%)		
Female	11 (52.4)	9 (56.3)
Male	10 (47.6)	7 (43.8)
BASELINE CHARACTERISTICS		
Efficacy-Evaluable NSCLC Subjects (n=16)		
Baseline ECOG Status, n (%)		
0		2 (12.5)
1		14 (87.5)
Disease Stage, n (%)		
III		4 (25.0)
IV		12 (75.0)
PD-L1 Status, n (%)		
PD-L1 ≥50%		1 (6.25)
PD-L1 ≥1 to <49%		7 (43.75)
PD-L1 <1%		4 (25.0)
Unknown		4 (25.0)
Actionable Mutation Status		
Wild-type		6 (37.50)
EGFR		2 (12.50)
KRAS		3 (18.75)
Unknown		5 (31.25)
Prior Therapy		
Median lines		2

RESULTS (COHORT 5)

Best Overall Response to Inhaled KB707

Efficacy-Evaluable[1] NSCLC Patients (n=16)	
Partial Response (PR)	5
Stable Disease (SD)	7
Progressive Disease (PD)	4
ORR	31.3%

[1] Subjects who received a minimum of one treatment cycle and with at least one post-baseline scan available for RECIST v1.1 response assessment per Investigator

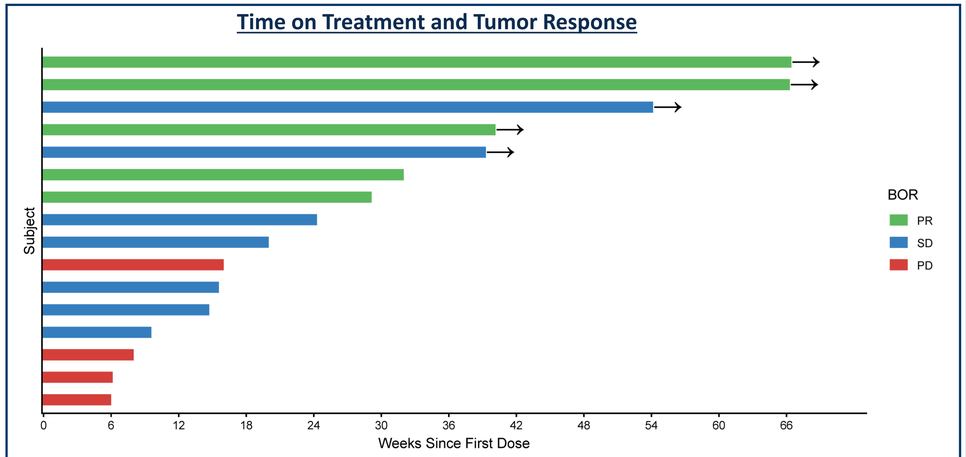
Inhaled KB707 Combination with Pembrolizumab is Safe and Well Tolerated

- Most TRAEs were Grade 1 or 2 and transient in duration.
- Patients experiencing ≥1 TRAE = 66.7% (14)
- One case of Grade 1 cytokine release syndrome

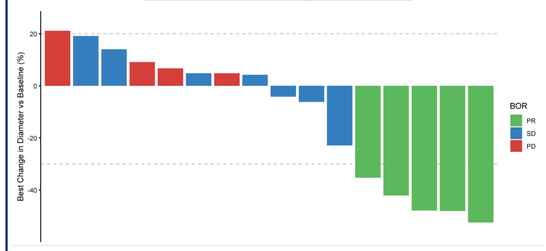
TRAE ≥5% Total Subjects in Safety Population (n=21)				
	Grade 1	Grade 2	Grade 3	Any n(%)
Dyspnea	0	5 (23.8)	2 (9.5)	7 (33.3)
Cough	0	1 (4.8)	1 (4.8)	2 (9.5)
Chills	2 (9.5)	0	0	2 (9.5)
Fatigue	2 (9.5)	0	0	2 (9.5)
Influenza-like Illness	0	2 (9.5)	0	2 (9.5)
Pyrexia	1 (4.8)	1 (4.8)	0	2 (9.5)
Vomiting	1 (4.8)	2 (9.5)	0	3 (14.3)
Nausea	2 (9.5)	0	0	2 (9.5)
Headache	1 (4.8)	0	1 (4.8)	2 (9.5)

Note: Subjects are counted once per preferred term at the highest severity level experienced.

Time on Treatment and Tumor Response



Reduction in Target Lesions



ACKNOWLEDGEMENTS

Krystal Biotech Inc. would like to thank all participating patients and their families, the investigators, and the site personnel. The authors also wish to thank Brittani Agostini, Molly Buch, Erica Butler, Shibani Kudchadkar, Rommel Hidalgo, Michael Johnston, Shashank Rana, Meghan Conner, and Ramakrishna Edukulla for their invaluable contributions.

The study was sponsored by Krystal Biotech, Inc. (Pittsburgh, PA, USA).
Additional information on clinicaltrials.gov (NCT06228326).
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