VISTA, PHASE 3 TRIAL OF VICINIUM, AN EPCAM-TARGETED PSEUDOMONAS EXOTOXIN, IN BCG-UNRESPONSIVE NON-MUSCLE INVASIVE BLADDER CANCER

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3rd edition GLOBAL CONGRESS ON BLADDER CANCER

BACKGROUND

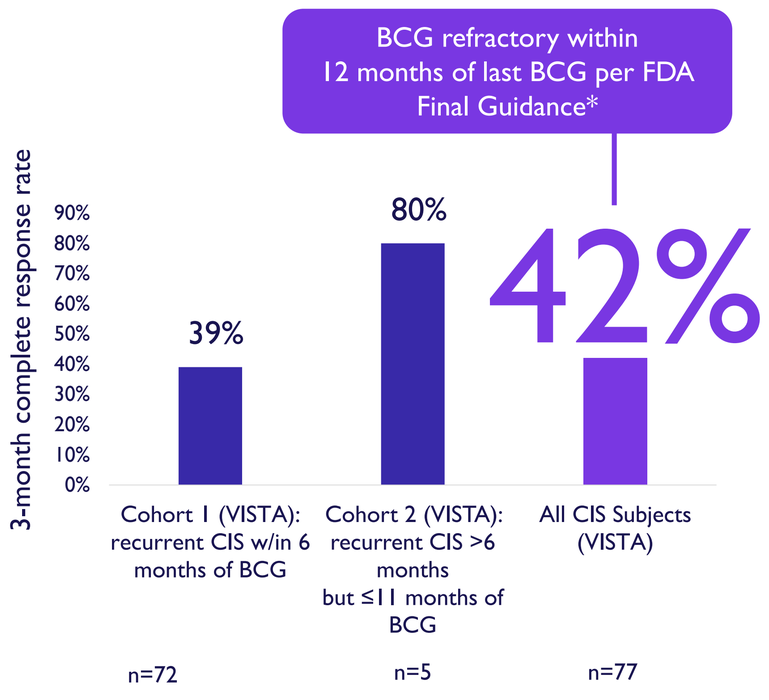
Vicinium is a fusion protein consisting of an Epithelial Cell Adhesion Molecule (EpCAM)-specific antibody fragment fused to *Pseudomonas* Exotoxin A, a potent inhibitor of protein synthesis. Vicinium is being developed for the treatment of Bacillus Calmette-Guérin (BCG)-unresponsive, high grade non-muscle invasive bladder cancer (NMIBC). In Phase 1 and 2 studies, intravesical Vicinium demonstrated excellent safety profile and meaningful clinical activity as assessed by the complete response (CR) rate at 3 months of 29-40% in subjects with carcinoma in situ (CIS) NMIBC. The major objective of this pivotal phase 3 study is to confirm the clinical benefit of Vicinium in subjects with BCG-unresponsive NMIBC.

ENROLLMENT & STUDY DEMOGRAPHICS

CHARACTERISTICS	COHORT 1	COHORT 2	COHORT 3
	CIS that recurred within 6 months of BCG	CIS that recurred >6 months but ≤11 months of BCG	Papillary (without CIS) that recurred within 6 months of BCG
Total subjects enrolled	87	6	40
Evaluable subjects at 3-months*	72	5	34
Median age (current)	75	71	77
Males/Females	54/18	4/1	29/5
Median prior treatment for NMIBC			
BCG cycles	4 (range 2-14)		
Intravesical chemotherapy	1 (range 0-23)		
TURBT	4 (range 0-11)		

*Data as of 20 April 2018 cut-off

3-MONTH CR RATE IN CIS



Data as of 20 April 2018 cut off
Efficacy assessment based on cystoscopy as well as centrally read cytology and, where suspicious lesions found on cystoscopy, central pathology
* BCG-Unresponsive Nonmuscle Invasive Bladder Cancer: Developing Drugs and Biologics for Treatment Guidance for Industry, February 2018

3-MONTH EFFICACY RESULTS IN PAPILLARY ONLY

68%

Recurrence-free rate at 3-months in papillary only subjects
(n=34)

Subjects deemed to have no visible evidence of disease when starting Vicinium treatment

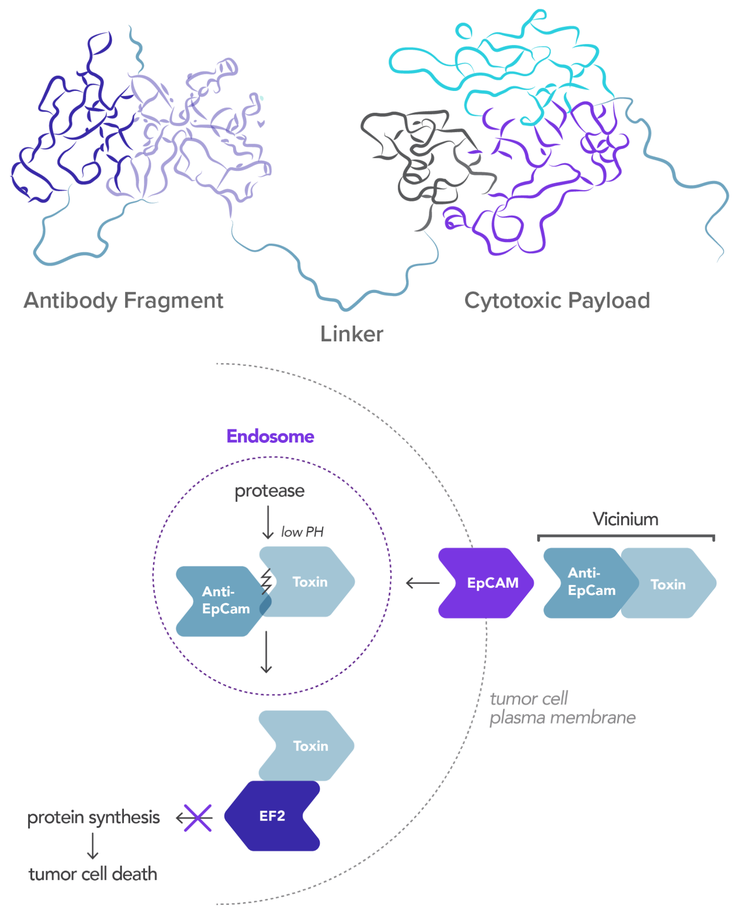
Data as of 20 April 2018 cut off

VICINIUM: NOVEL FUSION PROTEIN DESIGNED TO INCREASE TUMOR TARGETING AND DRUG SAFETY

- Engineered as a single fusion protein comprising an antibody fragment, peptide tether and cytotoxic payload
- Peptide tether allows fusion protein to remain intact until internalized by cancer cell; avoiding normal tissue by bladder cancer cells
- Anti-EpCAM Ab fragment delivers toxin that kills tumor cells by blocking protein synthesis
  - Kills both rapidly proliferating and slower growing cancer cells
- EpCAM overexpressed in >98% of high grade NMIBCs*, minimal expression on healthy bladder tissue
- Potential to induce immunogenic cell death

ETA: Pseudomonas exotoxin A
Potent: subpicomolar IC_{50}

* Data generated in prior Sesen BIO studies using internal antibody



VISTA TRIAL PHASE 3 STUDY DESIGN

- Single-arm, open-label, multi-center registration study in BCG-unresponsive NMIBC (high grade Ta, any T1 and CIS with or without papillary disease) (NCT02449239)
- Eligibility: ≥ 2 courses of full dose BCG and recurred with papillary NMIBC ≤ 30 weeks or with CIS ≤ 50 weeks after last BCG
- Dosing: 30mg Vicinium intravesical instillation in 50 ml buffered saline held for 2 hours
  Induction: biweekly for 6 weeks → weekly for 6 weeks; once CR, proceed to maintenance every other week for 2 years
- Primary endpoint: Complete response rate and duration of response in Cohort 1 (CR defined as negative urine cytology, pathology and local cystoscopy)
- Key Secondary Endpoints: event-free survival (EFS) in all subjects, time to disease recurrence, time to cystectomy, progression-free survival, overall survival, safety and tolerability

COHORT 1: CIS with or without papillary tumors that recurred within 6 months of BCG

COHORT 2: CIS with or without papillary tumors that recurred >6 months but ≤11 months of BCG

COHORT 3: Papillary tumors only that recurred within 6 months of BCG

BCG-unresponsive: completed 2+ courses (≥ 5 and ≥ 2 treatments resp.) of full dose BCG starting within 13 months of each other

TREATMENT-EMERGENT ADVERSE EVENTS

Treatment-Emergent Adverse Event[2]	Subjects (n=129) with: All TEAEs All Grades	All TEAEs Grade ≥3	Treatment-Related TEAEs All Grades	Treatment-Related TEAEs Grade ≥3[3]
Any TEAE	104 (81%)	36 (28%)	52 (41%)	5 (4%)
Urinary tract infection	37 (29%)	5 (4%)	13 (10%)	2 (%)
Dysuria	25 (19%)	0 (0%)	14 (11%)	0 (0%)
Hematuria	21 (16%)	2 (2%)	11 (9%)	0 (0%)
Pollakiuria (frequency of urination)	16 (12%)	0 (0%)	12 (9%)	0 (0%)
Diarrhea	13 (10%)	0 (0%)	2 (2%)	0 (0%)
Fatigue	13 (10%)	0 (0%)	8 (6%)	0 (0%)
Micturition urgency	11 (9%)	0 (0%)	8 (6%)	0 (0%)
Nausea	10 (8%)	1 (1%)	3 (2%)	0 (0%)
Lipase increased (all asymptomatic)	10 (8%)	4 (3%)	2 (2%)	1 (0%)

Subjects (n=129)	Treatment-Emergent SAEs[4]	Treatment-Related SAEs
Any Serious AE	17 (13%)	4 (3%)
Acute kidney injury or renal failure	4	3
Hematuria	3	0
Cholestatic hepatitis	0	1

1. <1% (n=4) treatment discontinuations due to AEs or progression of bladder cancer
2. Includes named TEAE and Lab Investigations occurring in more than 10 (8%) subjects regardless of treatment relationship
3. No grade 5 treatment-related adverse events observed
4. All SAEs that occurred in more than 1 subject

ALL SAMPLES SCREENED IN PHASE 3 TRIAL EXPRESS EPCAM

SCREENING EpCAM	
EpCAM Score	Number of Subjects
0	0
1+	12
2+	30
3+	29
TOTAL	71

FINAL EpCAM	
EpCAM Score	Number of Subjects
0	0
1+	3
2+	13
3+	7
TOTAL	23

Final EpCAM by TREATMENT FAILURE (at end of induction)

EpCAM Score	Number of Subjects
0	0
1+	3
2+	8
3+	3
TOTAL	14

Final EpCAM by DISEASE RECURRENCE (at time of recurrence)

EpCAM Score	Number of Subjects
0	0
1+	0
2+	5
3+	4
TOTAL	9

SUMMARY AND CONCLUSIONS

1. 3-month data from the VISTA Trial demonstrate 42% CR rate in subjects with CIS recurring within 12 months of last BCG treatment
   a. Confirmation of prior proof-of-concept data.
   b. Recurrence within 12 months of BCG is consistent with US FDA guidelines
   c. The novel mechanism of Vicinium coupled with the promising clinical benefit may provide an important alternative to existing therapies, including radical cystectomy.
2. Initial data in subjects with recurrent papillary-only NMIBC demonstrate 68% recurrence-free rate at 3 months.
3. The safety profile of Vicinium remains tolerable and manageable.
4. EpCAM, the molecular target of Vicinium, is nearly ubiquitously expressed in high-grade NMIBC. Additional biomarker analysis is in progress.
5. Vicinium has a familiar and convenient administration schedule similar to BCG-like instillation.