AHNS 12TH INTERNATIONAL CONFERENCE ON HEAD AND NECK CANCER

QUILT-3.100: Phase 1 Open-Label Study to Evaluate Safety and Determine the Maximum Tolerated Dose of IBRX-042 In Participants With HPV-Associated Head and Neck tumors

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DISCLOSURES

Travel paid for by ImmuniyBio

IBRX-042 HPV Vaccine Background

Human Adenovirus Vector Platform

hAd5 [E1-, E2b-, E3-] with 4 Ad5 deletions

1st Gen hAd5

- **E1:** induces the expression of other early genes; drives infected cells into S-phase, allowing viral DNA replication; oncogenic potential
- **E3**: involved in evading host immunity

Unique to IB platform

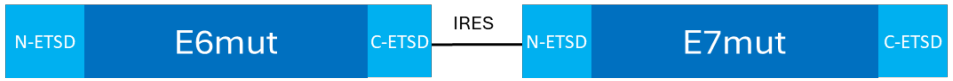
- **E2b**: **ΔpolI-** (adenovirus DNA polymerase) required for replication of the adenovirus genome;
- **E2b: ΔpTP-** (pre-terminal protein) required for viral replication

The hAd5 [E1-, E2b-, E3-] platform reduces expression of adenoviral structural proteins, enables homologous prime-boost regimens, and has been shown to drive antigen-specific responses in patients with pre-existing Ad5 immunity.

Wieking et al., 2012 *Cancer Gene Therapy*

IBRX-042: Targeting HPV16 E6 and E7 with the hAd5 [E1-, E2b-, E3-] platform

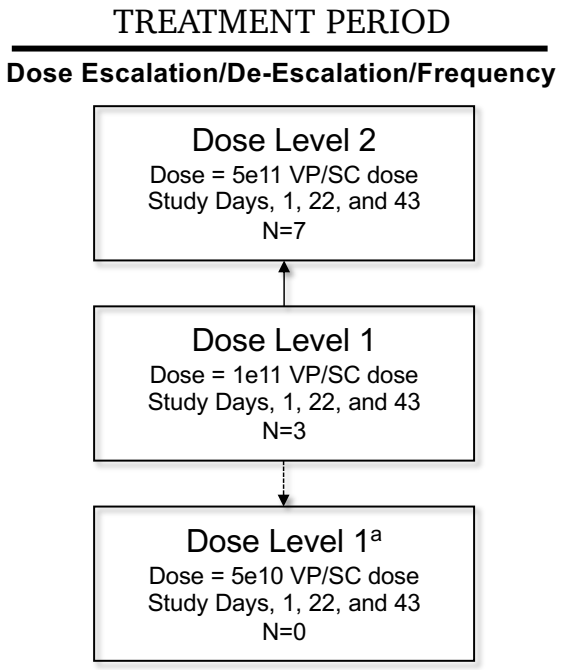
HPV16 E6 & E7 expression cassette



- ETSD sequences drive expression to endosomal pathway and enhance antigen-specific cellular responses
- E6mut contains mutations to prevent p53 and PTPN13 binding
- E7mut contains mutations to prevent Rb and Mi2β binding

Methods

- QUILT-3.100 was a phase 1, open-label study to evaluate the safety and to determine the MTD of IBRX-042 in participants with advanced/metastatic HPV-associated solid tumors.
  - All participants had at least one prior line of therapy
- IBRX-042 was administered subcutaneously every 3 weeks, for a total of 3 injections to participants with recurrent or progressive HPV-associated tumors.
- Determination of MTD used 3+3 dose escalation design:
  - Dose Level 1: 1e11 virus particles/dose
  - Dose Level 2: 5e11 virus particles/dose
- Participants were assessed for DLTs by safety review committee
- Immunogenicity was evaluated to examine HPV-specific peripheral T-cell and antibody



SC, subcutaneous; VP, viral particles.
[a] If needed, subjects will be enrolled into a de-escalation cohort at dose level -1 (dashed line, no patients enrolled)

Demographics

- 10 participants with HPV+ solid tumors were treated including 9 participants with H&N cancers.
- The highest administered dose was 5e11 virus particles and did not reach MTD
- No DLTs were observed
- No participants discontinued study treatment due to TEAEs

Demographics (N=10)		
Age (Median)	65.5	
Male (%)	80	
White (%)	70	
Squamous (%)	90	
ECOG 0 (%)	70	
Stage IV (%)	100	
Prior Therapy for metastatic disease (%)	90	
Prior exposure to checkpoint (%)	70	
Diagnoses (%)	Tonsil	50
	H&N	30
	Tongue	10
	Cervical	10

Safety/Results

CBC, Chemistry, Safety Data			
Laboratory Parameter (mean)	Time Point	Low Dose (n)	High Dose (n)
Hemoglobin (g/dL)	**Baseline**	13.93 (3)	12.57 (7)
	End of Treatment	14.70 (2)	12.42 (6)
Leukocytes (10^9/L)	**Baseline**	5.95 (3)	6.674 (7)
	End of Treatment	5.81 (2)	7.45 (6)
Lymphocytes (10^9/L)	**Baseline**	0.76 (3)	1.221 (7)
	End of Treatment	0.965 (2)	1.394 (5)
Neutrophils (10^9/L)	**Baseline**	4.377 (3)	4.404 (7)
	End of Treatment	3.795 (2)	4.762 (5)
Platlet (10^9/L)	**Baseline**	246.3 (3)	249.4 (7)
	End of Treatment	202.5 (2)	280.3 (6)
Hematocrit (L/L)	**Baseline**	41.47 (3)	37.44 (7)
	End of Treatment	43.9 (2)	37.55 (6)
ALT (U/L)	**Baseline**	31.3 (3)	22.4 (7)
	End of Treatment	28.5 (2)	25.5 (6)
AST (U/L)	**Baseline**	52.3 (3)	26.7 (7)
	End of Treatment	35.0 (2)	22.7 (6)
ALP (U/L)	**Baseline**	158.0 (3)	180.9 (7)
	End of Treatment	66.0 (2)	87.0 (6)

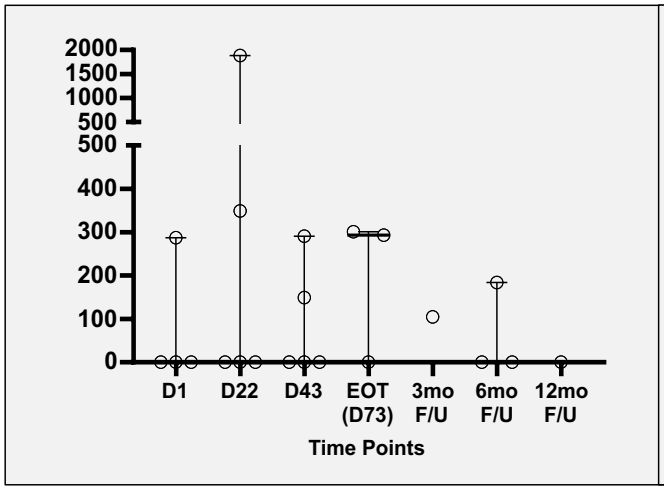
Treatment-Related Adverse Events N=10			
	Grade 1	Grade 2	Grade ≥3
Injection Site Pain	6	1	0
Myalgia	6	1	0
Injection Site Reaction	5	0	0
Injection Site Erythema	5	1	0
Fatigue	4	2	0
Injection Site Swelling	4	1	0
Chills	3	1	0
Injection Site Pruritus	2	0	0
Arthralgia	2	2	0
Diarrhea	2	0	0
Nausea	2	0	0
Headache	2	2	0
Pyrexia	1	0	0
Abdominal pain	1	1	0
Nasal Congestion	1	0	0
Rhinorrhea	1	0	0

Serious Adverse Events through month 6 after final vaccination N=10	
Pts with ≥1 SAE	3
Hemoptysis	2
Pleural Effusion	1
Respiratory Failure	1
Atrial Fibrillation	1
Disease Progression	1
Hypertension	1

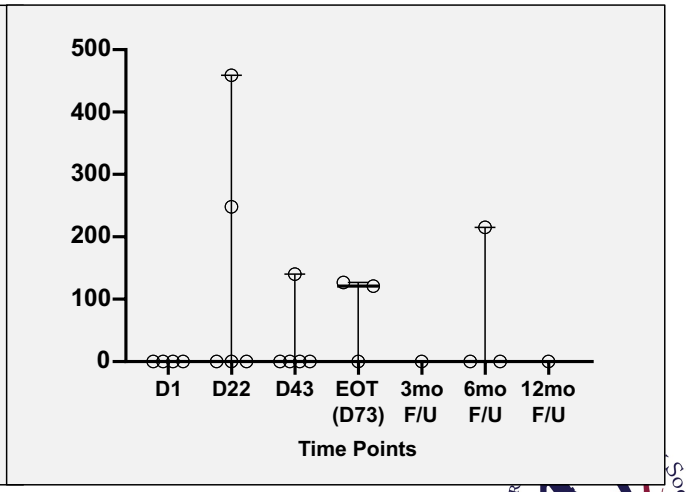
Cell-Mediated Immune Responses Against HPV After Vaccination with IBRX-042

- Elevated T-cell responses against both E6 and E7 were observed
- IBRX-042 induced immunity against HPV in study participants
- Immune responses against the HPV antigens were transient in nature as expected and in future studies, booster vaccinations with IBRX-042 may be administered to maintain immune surveillance against HPV

T-Cell Response to HPV16 E6 Antigen



T-Cell Response to HPV16 E7 Antigen



Note: SFC – Spot forming Cell

Conclusions

- The safety profile for HPV-directed cancer vaccine, IBRX-042, was well tolerated with no DLTs
- Cell-mediated immune responses against HPV were observed after vaccination with IBRX-042
- Results from this study support the development of ResQ-1190:
  - Phase 2 Study of NAI (IL-15 receptor agonist), HPV Vaccine (IBRX-042), and Nab-Paclitaxel in HPV-Positive Oropharyngeal Cancer Followed by De-Intensified Radiation Compared With Standard Chemoradiation (NCT07628062)
  - Status: Active; Site identification and activation

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Phase 2 ResQ-1190 Schema

Figure 1: Study Treatment Schema