

Title: DNA IMMUNOTHERAPY (INO-3107) INDUCES PERSISTENT IMMUNE RESPONSES RESULTING IN LONG-TERM EFFICACY THROUGH POST-TREATMENT YEAR 2 FOR HPV-6 & 11 RECURRENT RESPIRATORY PAPILLOMATOSIS

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Background: Recurrent respiratory papillomatosis (RRP) is a chronic disease caused by Human Papillomavirus (HPV-6/11). INO-3107, DNA immunotherapy designed to generate HPV-6/11 antigen-specific T-cells, was evaluated in a 52-week Phase I/II study (RRP-001, NCT04398433) and a retrospective, observational follow-up study (RRP-002).

Methods: RRP-001 eligibility included HPV-6 and/or 11 confirmed disease, requiring ≥ 2 RRP surgeries in the year preceding enrollment. Patients underwent surgical debulking within 14 days of Dose 1, then received INO-3107 on Day 0, Weeks 3, 6, and 9 via intramuscular injection. RRP-001 endpoints: safety and tolerability (primary), and post-INO-3107 surgical frequency and cellular immune responses (secondary). RRP-002 followed 28 of 32 patients (4 lost to follow-up) enrolled in RRP-001 for at least 52 additional weeks. RRP-002 assessments: surgical frequency and severe adverse events (SAEs).

Results: Mean annual surgeries were reduced by 59% by in Year 1 (Y1; RRP-001) (Figure). Immunology analyses at Y1 of patients with sufficient samples showed 73% (19/26) exhibited persistent significantly expanded T-cell populations assessed by TCR β sequencing of peripheral blood, and 71% (12/17) exhibited CD8⁺ Effector Memory T-cell enrichment assessed by RNA sequencing of airway tissue. Mean annual surgeries further declined in Year 2 (Y2) by 78% compared to pre-treatment. 86% (24/28) of patients experienced a 50-100% surgery reduction in Y2, an increase from 72% (23/32) in Y1 (Table). INO-3107 was well-tolerated with no treatment-related long-term SAEs.

Figure: Mean Surgical Reduction

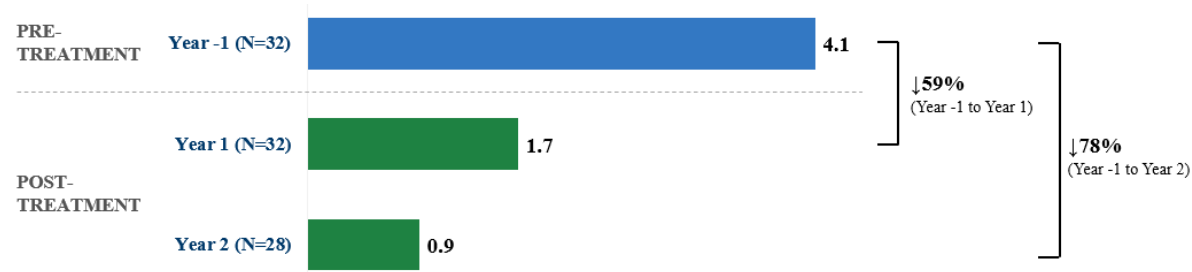


Table: INO-3107 Clinical Response

Parameter (surgery reduction compared to pre-treatment period)	Year 1	Year 2
Overall Response Rate:	72%	86%
% patients with 50-100% reduction	(23/32)	(24/28)
Complete Response:	28%	50%
% patients with 100% reduction	(9/32)	(14/28)
Partial Response:	44%	36%
% patients with 50-99% reduction	(14/32)	(10/28)

Conclusion: DNA immunotherapy INO-3107 demonstrates a continued clinical effect with further surgery reduction seen over time supported by generation of a long-lasting antigen-specific T-cell response in recurrent respiratory papillomatosis patients.