Interim Analysis of a Prospective Trial of Upright Image-Guided Proton Therapy for Recurrent Lung, Brain, and Head and Neck Malignancies

Philip Blumenfeld, Alexander Pryanichnikov, Marcel Fang, Ayman Salhab, Yair Hillman, Eduard Arbit, Ella Wajnryt, Aviad Berger, Jon Feldman, Aron Popovtzer

Hadassah Medical Center, Hebrew University of Jerusalem

P-Cure Ltd./Inc.

Purpose/Objectives

Upright image-guided proton therapy (IGPT) enables fixed-beam proton delivery without a rotating gantry, potentially reducing facility complexity while preserving dosimetric and clinical performance. This prospective trial evaluates the feasibility, safety, and early clinical outcomes of upright IGPT in patients with recurrent lung, brain, and head and neck (H&N) malignancies. We report an interim analysis at 50% of planned accrual.

Materials/Methods

This prospective study enrolled adult patients with recurrent or previously irradiated malignancies treated using upright pencil-beam scanning IGPT at a single institution. Patients were treated in a seated position using a robotic patient positioning system with a carbon-fiber chair, integrated vertical CT imaging, and daily volumetric (pre-irradiation) and planar (intra-irradiation) image guidance. The current interim analysis includes 50 patients: lung (n = 15), brain (n = 10), and H&N (n = 25). Treatment response was assessed at first follow-up using standard imaging criteria. Radiation-induced and/or treatment device–related acute toxicity was graded according to CTCAE v5. Descriptive statistics were used for analysis.

Results

At 3-month follow-up, best overall response among 50 patients was complete response (CR) in 40% (20/50), partial response (PR) in 18% (9/50), and stable disease (SD) in 18% (9/50); progressive disease was observed in 2% (1/50). Six patients (12%) died prior to the 3-month assessment, four patients (8%) were not evaluable due to incomplete follow-up, and one patient (2%) withdrew from the study (Table 1).

Acute toxicities were predominantly low grade. The most common CTCAE-grouped events (Table 1) were fatigue (42%), pain (26%), dysphagia/oral pain (24%), nausea (14%), dermatitis/erythema (12%), headache (12%), alopecia (10%), and cough (10%). Grade ≥3 acute toxicities were uncommon (6%).

Conclusions

Based on the current interim results, upright image-guided IGPT appears feasible and well tolerated across multiple disease sites, with encouraging early tumor response and

a favorable acute toxicity profile. These findings support continued enrollment and further evaluation of this approach as a potentially cost-efficient and clinically viable proton therapy delivery paradigm.

Table 1. Patient status by treatment site at 3-month follow-up and accute toxic effects CTCAE v5 (n = 50)

Outcome	**Head & Neck (n = 25)**	**Brain (n = 10)**	**Lung (n = 15)**
Complete Response (CR)	16	0	4
Partial Response (PR)	3	1	5
Stable Disease (SD)	2	5	2
Progressive Disease (PD)	0	1	0
Died	4	1	1
Not evaluable	0	1	3
Withdrew from study	0	1	0
Acute toxicity (n = 50)	**Grade 1**	**Grade 2**	**Grade ≥ 3**
Fatigue (50)	34% (17)	6% (3)	2% (1)
Pain (general) (50)	8% (4)	18% (9)	0% (0)
Dysphagia / oral pain (50)	12% (6)	10% (5)	2% (1)
Nausea (50)	12% (6)	2% (1)	0% (0)
Dermatitis / erythema (50)	6% (3)	6% (3)	0% (0)
Headache (50)	8% (4)	2% (1)	2% (1)
Alopecia (50)	8% (4)	2% (1)	0% (0)
Headache (50)	8% (4)	2% (1)	2% (1)
Alopecia (50)	8% (4)	2% (1)	0% (0)
Cough (50)	6% (3)	4% (2)	0% (0)
Flu-like symptoms (50)	4% (2)	0% (0)	0% (0)
Mucositis (50)	0% (0)	2% (1)	0% (0)