Synoptic Clinical Study Report	
Drug Substance	Durvalumab
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Prospective, Interventional Pilot Study of Mobile Devices and Digital Applications to Detect Early Pneumonitis and Other Pulmonary Adverse Events in Unresectable Stage III Non-Small Cell Lung Cancer Patients on Durvalumab (ON TRAX Study)

Study dates:	First subject enrolled: 22 October 2020 Last subject last visit: 16 February 2022 The analyses presented in this report are based on a clinical data lock date of 05 May 2022
Phase of development:	Pilot study
Sponsor's Responsible Medical Officer:	PPD Gaithersburg, MD 20878

This study was performed in compliance with International Council for Harmonisation (ICH) Good Clinical Practice, including the archiving of essential documents.

3. SYNOPSIS

Study centre(s)

The ON TRAX pilot study was conducted at 25 sites in the United States.

Publications

None at the time of writing this report.

Objectives and criteria for evaluation

Table S1 Objectives and Endpoints

Objectives	Endpoints
Primary	
• Describe the identification of treatment-emergent pneumonitis by grade in patients with unresectable Stage III non-small cell lung cancer (NSCLC) receiving durvalumab through the use of mobile technology	• Occurrence of pneumonitis, by grade • Grade of pneumonitis at diagnosis and highest grade of pneumonitis
Secondary	
• Describe durvalumab treatment discontinuation due to pulmonary adverse events (AEs), including pneumonitis	• Permanent discontinuation of durvalumab due to pulmonary AEs, including pneumonitis
• Describe the duration of durvalumab use	• Duration (days) of durvalumab treatment • Early discontinuation of durvalumab treatment for any reason • Treatment interruptions, duration (days) of interruptions, and the reason for interruptions
• Describe the incidence of pulmonary AEs by grade	• Occurrence of pulmonary AEs, including diagnoses of events, by grade • Duration (days) of pulmonary AEs by type and grade
• Describe the severity of pulmonary AEs (including pneumonitis) and use of medication to manage AEs	• Prescription of medication used to manage pulmonary AEs and duration (days) of treatment

• Describe the time to development of Grade 3 to 5 AEs, including pneumonitis	• Time (days) to development of Grade 3 to 5 AEs, including pneumonitis
• Describe health-related quality of life (QoL) during the study and its relationship with AEs	• Change in QoL scores from baseline
Exploratory	
CCI	

Study design

ON TRAX was a multicenter, prospective, interventional pilot study of mobile devices and digital applications aimed to detect early signs of pneumonitis and other pulmonary adverse events that was conducted in the United States. It included patients with unresectable Stage III Non-Small Cell Lung Cancer (NSCLC) who were treated with durvalumab per standard of care (SoC) for up to 12 months or until confirmed disease progression, unacceptable toxicity, permanent discontinuation of durvalumab, the initiation of alternative cancer therapy, death, or withdrawal of consent, whichever was soonest. After the clinical decision of recommending durvalumab had been made and acceptance from patients, study personnel presented this pilot digital technology study to patients. During the initial screening, patients consented that they were willing and able to use the mobile application and connected devices daily for up to 12 months, as well as complete quality-of-life (QoL) assessments for the duration of the study. Enrolled participants initiated durvalumab treatment within 2 weeks of the baseline visit, including on the same day, and study visits coincided with routine SoC visits to minimize intrusions in their treatment journey. Patients received mobile and wearable devices while on SoC treatment with durvalumab (not part of the study) without any additional interventions.

Target population and sample size

The planned study population was to be comprised of 75 patients with unresectable Stage III NSCLC whose disease had not progressed following 2 or more cycles of platinum-based chemotherapy given concurrently with radiation therapy (concurrent chemoradiotherapy [cCRT]) and who were eligible to receive durvalumab, as outlined in the package insert. Patients were recruited at 25 study sites in the United States. Due to a variety of factors including the COVID-19 pandemic, shortage of staff, and limited access to sites, 46 patients were consented and screened for inclusion in the study before early termination of the study. Patients needed to be onboarded with the devices and receive at least 1 dose of durvalumab. Of those 46 consented patients, 6 did not meet eligibility criteria for the study. This resulted in a final sample size of 40 patients.

Investigational product and comparator(s): dosage, mode of administration and batch numbers

ON TRAX was a pilot study investigating the feasibility of the Current Wearable Health Monitoring System to detect early signs of pneumonitis and other pulmonary AEs while patients were undergoing SoC durvalumab treatment. The Current Wearable Health Monitoring System was comprised of a multiparametric wearable device to be worn continuously strapped around the arm, a mobile spirometer, and a tablet. The system provided continuous remote monitoring of patient health measures, such as vital signs (skin temperature, heart rate, respiratory rate), oxygen saturation (pulse oximetry) and physical movement (number of steps per day). Mid-study, the wearable device was upgraded from generation 1 to generation 2, a much smaller and lighter device with the same capabilities. The system also collected daily pulmonary function tests (spirometry) and patient reported outcomes (PROs) at predefined timepoints. Qualified site personnel had real-time access to all collected data, except for PROs, via a web-based or a mobile app dashboard and received notifications when pre-set conditions were met. Real time monitoring of the dashboard by independent triage nurses was implemented towards the end of the study. All potential intervention decisions were left with the treating physician and no specific diagnosis or treatment recommendations were provided.

Durvalumab was not supplied as part of this digital technology study. Investigators administered durvalumab per the package insert recommendations.

Duration of treatment

Patients were monitored remotely with the Current Health System while undergoing SoC durvalumab treatment up to 12 months or until withdrawal of study consent, whichever occurred sooner. All patients received at least one dose of durvalumab and investigators used their clinical judgement in SoC durvalumab treatment management. Durvalumab treatment patterns and AEs reported here were captured only while patients participated in this pilot digital technology study. There were some patients who withdrew study consent and continued with their SoC durvalumab treatment. Also, the study was terminated early and patients continued on their SoC durvalumab treatment. Out of the 40 patients in the study, there were 3 patients who discontinued durvalumab early due to disease progression. The duration of durvalumab treatment while on study ranged from 1 day to 352 days, with a mean length of 107.5 days.

Statistical methods

Data analyses for the endpoints were descriptive, with no formal statistical testing, among all patients in the safety analysis set. The occurrence of pulmonary AEs by type and grade according to Common Terminology Criteria for Adverse Events (CTCAE) v5.0 were summarized descriptively, using frequencies and percentages. Continuous endpoint variables were summarized by the number of observations, mean, standard deviation, median, minimum, maximum, and 95% confidence interval (CI). Categorical variables were summarized by frequency counts and percentages for each category. The safety analysis involved examination of the descriptive statistics and individual patient listings for clinical tolerability and safety by overall patients in the safety analysis set. Summaries of treatment-emergent adverse events (TEAEs) included the events by system organ class and preferred term, events by maximum severity, events by possible relationship to study treatment, events leading to study discontinuation, and serious adverse events (SAEs).

Study population

The study population included 40 patients with unresectable Stage III NSCLC who were recruited at 25 study sites in the United States, although only 16 sites enrolled at least 1 patient. Of the 46 patients who were screened for participation in the study over 22 months, 6 patients did not meet all inclusion criteria. Of the 40 patients who enrolled in the study, 5 completed the study and 35 discontinued the study early. The most common reason for study discontinuation was early termination of the trial (N=19), which occurred on January 31, 2022. The data cut off was May 5, 2022.

The mean age of patients was 65.1 years (standard deviation [SD] = 8.9 years) with over half (52.3%) being 65 years old or older. The majority of study participants (60%) were male. Other baseline characteristics that were captured via investigator assessment and wearable device are included in Table 14.1.3.

Summary of safety results

Overall, 30 patients (75%) experienced any TEAE, including device-related AEs, and 5 patients (12.5%) experienced a TEAE with a grade of 3 or higher, of which 1 patient (2.5%) experienced a TEAE (disease progression) with an outcome of death. TEAEs were defined as any AEs, irrespective of causality, which occurred or worsened at any time after the start of administration of the first dose of durvalumab and through 30 days after the last dose of durvalumab, while patients participated in this pilot study. There were 4 patients (10%) who had a TEAE considered possibly related to the medical device, 2 of which resulted in study discontinuation (5%). There were 15 patients (37.5%) who experienced a TEAE which led to an interruption of durvalumab treatment and 2 patients (5%) whose TEAE led to the discontinuation of durvalumab.

CCI [redacted] Two of

the 3 pneumonitis TEAE cases were reported as possibly related to durvalumab and both patients were treated with high dose prednisone.

Conclusion(s)

The ON TRAX pilot study consisted of 40 patients with unresectable Stage III NSCLC who received at least one dose of durvalumab per SoC. The first site was activated in March 2020 and the study was terminated early in January 2022. Patients used wearable technology, a portable spirometer, and a mobile application to record vital signs, respiratory data and PROs that may aid in early detection of pneumonitis and pulmonary AEs. There were 30 patients (75%) who experienced one or more TEAEs, with 5 patients (12.5%) experiencing severe or life-threatening TEAEs (≥ grade 3). There were 4 patients (10%) with a TEAE possibly related to the medical device and 2 (5%) of them discontinued the study due to this type of AE. Three patients (7.5%) experienced a TEAE of pneumonitis. CCI [redacted]

Limitations of this pilot study include the small sample size, limited number of patients who experienced pneumonitis, patient adherence and retention challenges related to the technology, and early termination of the trial. Due to these reasons, there was limited potential to assess the feasibility of early detection of pneumonitis with this technology. Additional studies with a more robust patient population with longer follow-up and more user-friendly technology may be appropriate. The initial device was very large and had a specific orientation for use. More modern, smaller devices are now available which may improve patient adherence and retention in future studies. As more patients use the monitoring system, a future study may be able to better understand whether the devices and application identify early signs of pneumonitis and other pulmonary AEs.