Transition from TD300 Inhalation Device to Dry-Powder Inhaler for Treprostinil Administration: Comparing Dosing, Tolerability, and Reason for Conversion

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ABSTRACT

OBJECTIVE: Evaluate tolerability, patient reported adverse events, and reason for conversion in patients who utilized a TD300 inhalation device and then transitioned to a dry-powder inhaler (DPI) to administer inhaled treprostinil.

DESIGN: Retrospective, crossover comparison of patients on inhaled treprostinil who utilized the TD300 device for at least 12 months before converting to a DPI and used the inhaler for at least 6 months.

METHODS: A review of the electronic medical records was conducted to evaluate patient maintenance dose post conversion, reported reason for conversion, and patient reported adverse events related to patients using inhaled treprostinil for Pulmonary Arterial Hypertension (PAH) treatment.

Inclusion criteria included patients aged 18 thru 89 and carried a diagnosis of either World Health Organization (WHO) Group 1 PAH or WHO Group 3 Pulmonary Hypertension (PH) associated with interstitial lung disease (ILD). Patients were included if they completed 12 months of therapy using a TD300 device followed by 6 months using a Dry-Powder Inhaler (DPI). Patients started inhaled treprostinil via a TD300 inhalation after March 2, 2020 and the DPI after July 20, 2022.

Exclusion criteria included any patient who displayed a gap in therapy at any point during the review period or who transitioned more than one time from a TD300 device to DPI or from a DPI to the TD300 device.

Records were reviewed to interpret the reason for transition, dose equivalence on conversion to DPI, and patient reported adverse events experienced on either inhalation device.

RESULTS: The sample size of 32 patients reviewed showed that 91% (29/32) of patients initiated a conversion to DPI due to ease-of-use (78% [25/32] for convenience and 13% [4/32] due to desire for less complex regimen). Three patients (9% [3/32]) resulted in an unknown reason for transition.

Twenty-one patients (66% [21/32]) were able to convert to an equivalent treprostinil dose and frequency using the DPI. Six patients (19% [6/32]) were able to achieve a higher dose upon transition and five patients (15% [5/32]) achieved a lower maintenance dose.

Side effect data was collected for both inhalation devices for the first 6 months the patient was on service with each device. While on the TD300 device, the most common side effects (>10%) included cough, headache, increased shortness of breath, diarrhea, congestion, dizziness, hypotension, nausea, muscle/joint pain, upset stomach, and edema.

Administration with a DPI resulted in side effects (>10%) aligning with those in the Package Insert, including cough, increased shortness of breath, congestion, and edema.

CONCLUSIONS: Conversion from a TD300 inhalation device to a Dry-Powder Inhaler was well-tolerated with a majority of patients achieving an equivalent dose of inhaled treprostinil. This coupled with the reported ease-of-use advantage of the DPI makes transitioning a viable option for patients treating PAH and PH-ILD with inhaled treprostinil.

COMMERCIAL SUPPORT GRANT DISCLOSURE: Research funded solely through Accredo Health Group, Inc. with no outside commercial support to disclose.

METHODS

On transition from TD300 to DPI for administration of treprostinil, the patient receives comprehensive counseling from a PAH specialist pharmacist. During this discussion, the patient reported reason for transitioning from one device to the other is captured and documented in the electronic medical record.

All patients receive training by a PAH-specialist nurse on initiation of each device, including in-home training on their first day of therapy.

Patients are engaged telephonically each month by a non-clinician. During this scheduled monthly re-order, the patient is asked non-interpretive questions designed to screen for potential adverse events (AEs). If answers are suggestive of an AE, the patient is triaged to a PAH specialist clinician for further evaluation. This clinical patient engagement is documented in the electronic medication record.

A manual review of each eligible patient's electronic medical record drove the capture of patient reported AEs. A patient may have reported a particular AE multiple times within the 6 month timeframe of either cohort, however the data was limited to a specific reported event one time per AE per cohort. A data collection tool was utilized to accurately track patient reported AEs for patients utilizing the TD300 Inhalation device and the Dry Powder Inhaler. One pharmacist reviewed all patient reported adverse events.

The patient's dose while utilizing the TD300 device was compared to inhaled treprostinil dose at initiation of therapy with the dry-powder inhaler. Figure 1 displays dose equivalence between the inhalation devices along with the DPI cartridge color associated with each strength.

Figure 1: Equivalent Conversions by Dose

DPI Cartridge Color	DPI Cartridge Strength	TD3D0 Device Number of breaths
	16 mcg	</= to 5
	32 mcg	6 to 7
	48 mcg	8 to 10
	64 mcg	11 to 12

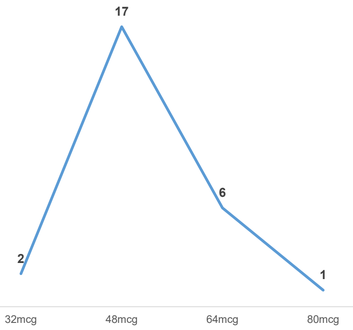
adapted from manufacturer training document

A manual review to compare the length of the nursing visit on day one of treprostinil initiation for each device was completed by a PAH specialist nurse. The results of this review were validated by two additional nurses trained on the PAH disease state.

Training included the use and maintenance of each device and disposables, disease education, and measures to ensure optimal compliance and adherence to therapy.

RESULTS

Figure 2: Equivalent Conversions by Dose



Most patients (91% [29/32]) provided a reason for conversion related to ease-of-use. Figure 4 displays each patients primary reason for transitioning to the DPI.

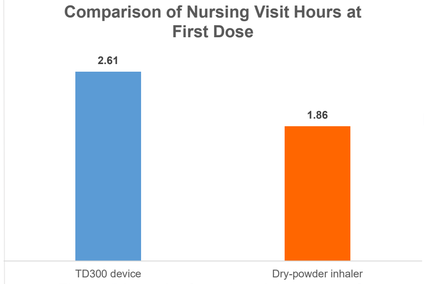


Figure 5 Length of nursing visit at start-of-care

Figure 3 shows the number of patients diagnosed with WHO Group 1 PAH or WHO Group 3 Pulmonary Hypertension (PH) associated with interstitial lung disease (ILD).

Twenty-six (81% [26/32]) patients achieved a treprostinil DPI maintenance dose equivalent to the established TD300 device maintenance dose at time of conversion (figure 2). Four (15% [4/26]) patients that converted to an equivalent dose were able to further increase their dose.

For these four patients, the average number of days between the first DPI shipment and the patients increased treprostinil dose equaled 109 days (range of 42 to 147 days).

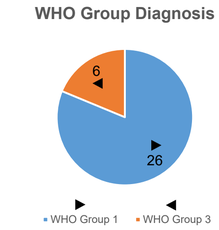


Figure 3: WHO Group Diagnosis

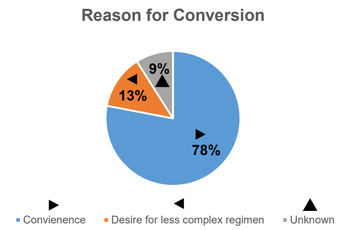


Figure 4: Reason for Conversion

A difference in amount of time used for patient training at initiation of conversion was noticed. Patients starting on the TD300 device required an average of 156 minutes (2.81 hours) for nurse training to be completed, compared to an 113 minute (1.88 hours) average for patients starting on the DPI device (figure 5).

Figures 6 and 7 demonstrates patient reported AEs that occurred greater than 10% while utilizing either the TD300 inhalation device or the Dry-powder inhaler. These AEs align with expected treprostinil side effects reported in the Package Inserts.

AEs were comparable between WHO Group 1 and WHO Group 3 patients. 33% (2/6) WHO Group 3 patients reported cough while utilizing the TD300 and DPI.

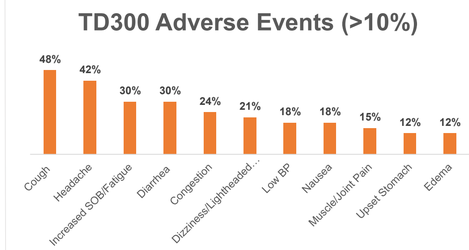


Figure 6: TD300 Adverse Events

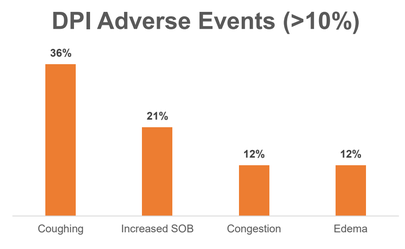


Figure 7: DPI Adverse Events

REFERENCES

1. *Tyvaso®* [package insert]. Research Triangle Park, NC: United Therapeutics; 2023.
2. *Tyvaso® DPI* [package insert]. Research Triangle Park, NC: United Therapeutics; 2023

CONCLUSIONS

Evaluation of the sample size proved that most patients were able to achieve equivalent treprostinil maintenance doses on conversion to a dry-powder inhaler while tolerating therapy and enhancing ease-of-use. PAH specialist nurses provided a level of knowledge and expertise that allowed patients to convert to an alternate device with no interruptions or gaps in care. Limitations to the study include not evaluating the excluded patients that may have converted back to the TD300 inhalation device prior to reaching 6 months of service on the DPI and also the sample size was not large enough to establish clinical significance.