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Transitions between intravenous (IV) or subcutaneous (SQ) and oral prostacyclin pathway agents (PPAs) in pulmonary arterial hypertension (PAH): Four case reports

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Background: PPAs are a critical first-line treatment for patients with moderate to severe PAH and are frequently used in combination with other PAH therapies. The first PPAs to receive FDA approval required continuous IV or SQ administration delivery route associated with safety and tolerability drawbacks, including infection, sepsis, bleeding, site abscess, site reaction, and pain. Seven PPAs are now available, including agents administered IV/SQ, by inhalation, and orally; PAH patients are now transitioned from one PPA to another with increasing frequency. Such transitions require careful down- and up-titration to avoid rebound effects from rapid withdrawal, and to achieve a patient's individual optimal dose based on efficacy and tolerability. Clinical guidance is especially lacking for transitions involving oral PPAs: oral treprostinil (Orenitram) and selexipag (Uptravi).

Methods: We present 4 case reports of PAH patients who transitioned between IV/SQ and oral PPAs at our institutions.

Results: Patient 1 had functional class IV symptoms at diagnosis, but improved with upfront combination therapy (ambrisentan, sildenafil, IV epoprostenol [Veletri]). Due to repeated line infections, he transitioned to selexipag, and remains stable after 35 months. His case illustrates that patients with initially severe disease can be stabilized with combination therapy to the point where transition to an oral PPA is feasible. Patient 2 experienced infusion site pain on SQ treprostinil (Remodulin), so was transitioned to oral treprostinil, with initial success. After 7 months, she was urgently transitioned back to SQ treprostinil, due to worsening symptoms. Side effects had prevented her from reaching an effective oral treprostinil dose, contributing to disease worsening. Patient 3 was on selexipag for 10 months before being hospitalized for urinary tract infection and septic shock. While intubated, she was emergently transitioned to IV epoprostenol and IV sildenafil; upon recovery, she transitioned back to selexipag, and remains stable after 5 months. Her case illustrates the importance of background therapy during transitions, and the growing reality that as PAH patients survive longer, they may require multiple transitions between PPAs. Patient 4 transitioned from selexipag to IV treprostinil, in order to be listed for a liver transplant (biliary cirrhosis). She was hospitalized, transitioned successfully despite PPA side effects (nausea and vomiting), and continued slower up-titration to an effective dose following discharge. Her case suggests the possible need for a slower up-titration in patients transitioning away from selexipag, because of a potential for increased side effects when overlapping PPAs.

Conclusions: These cases will be presented in greater detail at the PHPN Symposium, allowing exploration of the practicalities of transitioning patients such as patient selection, titration protocols, and dose equivalence.



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