It is unknown whether darunavir is secreted in human breast milk. Preclinical studies demonstrated that the drug is secreted in the milk of lactating rats. Due to the potential risk of HIV transmission to the infant, in addition to the potential for unknown adverse reactions, it is recommended that darunavir is not prescribed in this setting.

7f. Use in pediatrics

DIONE

Darunavir has been studied as initial therapy in HIV-infected adolescents aged 12–18 years in DIONE, an open label, phase II, single arm study (Flynn *et al.*, 2014). A total of 12 participants, across six sites, were administered once-daily ritonavir-boosted darunavir at 800/100 mg in combination with an NRTI backbone of either zidovudine–lamivudine or abacavir–lamivudine. 92% of participants at 24 weeks and 83% at 48 weeks had achieved a viral load of l< 50 copies/ml. Darunavir was generally well tolerated in this group.

Darunavir has been studied in treatment-experienced children and adolescents in two open-label, single-arm trials.

DELPHI

In DELPHI (Blanche *et al.*, 2009), a study of highly treatment experienced children and adolescents aged 6–17 years, many with preexisting protease inhibitor RAMs, twice-daily boosted darunavir was administered together with an optimized background regimen. At 48 weeks, 48% of patients had achieved virologic suppression. Of the 24 patients who experienced virologic failure, over 10% developed DRV associated major protease inhibitor mutations.

ARIEL

ARIEL was a study of younger, treatment-experienced children aged 3–6 years of age who received twice-daily darunavir with ritonavir (20/3 mg/kg, with doses then adjusted to 25/3 mg/kg twice daily for patients weighing < 15 kg, and 375/50 mg twice daily for those weighing between 15 and 20 kg) plus an investigator-selected optimized background regimen (Violari *et al.,* 2015). At 48 weeks, 17 of 21 patients (81%) had a suppressed viral load < 50 copies/ml. Three virologic failures occurred by 48 weeks. Paired baseline and end point phenotypic resistance testing was available for 2 of these patients, and no treatment-emergent resistance to darunavir or the agents in the background regimen was found.

The DHHS (2015b) treatment guidelines recommend boosted darunavir, together with an NRTI backbone, as a preferred protease inhibitor regimen in children 3 years of age or older and adolescents.

7g. Boosted darunavir monotherapy as a simplification strategy

Switching from a regimen of twice-daily darunavir boosted with ritonavir (600/100 mg) plus two other antiretroviral drugs with less than two darunavir-associated resistance mutations in patients with virologic suppression to a once-daily darunavir–ritonavir (800/100 mg) regimen or to maintain their current regimen resulted in greater virologic suppression in the once-daily arm versus twice-daily arm (90% va. 83.3%, respectively), and with a significantly greater reduction in LDL levels in the once-daily arm (−8 mg/dl vs +3.3 mg/dl; p = 0.04) and better adherence, in the DRIVESHAFT study (Huhn *et al.,* 2015).

The comparative efficacy and safety of boosted darunavir or boosted lopinavir monotherapy was investigated as a simplication strategy in 75 patients. Of the 305 patients, 155 received the darunavir regimen. In the intent-to-treat analysis 77.5% of those receiving darunavir and 66.6% of those receiving lopinavir had sustained virologic suppression at 48 weeks. No patient in the darunavir arm developed virologic failure; the discontinuation rate in this arm due to adverse events was 15% versus 18.2 % of patients receiving lopinavir (Santos *et al.,* 2016).

7h. Postexposure prophylaxis

Patients with documented or potential HIV exposure, either occupational or sexual, were enrolled within 72 hours of exposure into PEPDar and randomized to receive ritonavir-boosted darunavir plus two NRTIs or standard of care treatment. Early discontinuation rate was 6.5% versus standard of care (10.0%). Noninferiority of the darunavir-containing regimen to standard of care was reported (Fatkenheuer *et al.*, 2016).

Acknowledgment: The previous version of this chapter, published in the 6th edition of *Kucers' The Use of Antibiotics*, was co-written by Anne Mijch, of the Department of Medicine, Monash University and Victorian HIV/AIDS Service, Alfred Hospital in Melbourne, Australia. Her contribution was substantial and much appreciated.

REFERENCES

Almudimeegh A, Rioux C, Ferrand H *et al.* (2014). Drug reaction with eosinophilia and systemic symptoms, or virus reactivation with eosinophilia and systemic symptoms as a manifestation of immune reconstitution inflammatory disease in a patient with HIV? *Br J Dermatol* **171**: 895.

Antinori A, Clarke A, Svedhem-Johansson V *et al.* (2015). Week 48 efficacy and central nervous system analysis of darunavir/ritonavir monotherapy versus darunavir/ritonavir with two nucleoside analogues. *AIDS* **29**: 1811.

APRegistry (2015). Antiretroviral Pregnancy Registry International interim report for 1 January 1989 through 31 July 2015. apregistry.com/forms/interim_report.pdf. Accessed 3 June 2017.

Arasteh K, Yeni P, Pozniak A *et al.* (2009). Efficacy and safety of darunavir/ritonavir in treatment-experienced HIV type-1 patients in the POWER 1, 2 and 3 trials at week 96. *Antivir Ther* **14**: 859.

Arribas JR, Clumeck N, Nelson M *et al.* (2012). The MONET trial: week 144 analysis of the efficacy of darunavir/ritonavir monotherapy versus plus two nucleoside reverse transcriptase inhibitors, for patients with viral load <50 copies/ml at baseline. *HIV Med* **13**: 398.

Arribas JR, Horban A, Gerstoft J *et al.* (2010). The MONET trial: darunavir/ritonavir with or without nucleoside analogues, for patients with HIV RNA below 50 copies /ml. *AIDS* **24**: 223.

ASHM (2015). Antiretroviral guidelines: US DHHS guidelines with Australian commentary. arv.ashm.org.au/arv-guidelines/the-australian-commentary-index. Accessed 3 June 2017.