**Recommendations for CNI/mTOR Management with Paxlovid Coadministration**

* Paxlovid
  + Indicated to treat mild-moderate COVID19 infection initiated within 5 days of symptom onset
  + Dosing: 3 tablets (Nirmatrelvir 300 mg with ritonavir 100 mg) twice daily x 5 days
    - Renal adjustments
      * CrCl 30-59: 2 tablet combination twice daily x 5 days [150 mg nirmatrelvir (1 tab) plus 100 mg ritonavir (1 tab)]
      * CrCl < 30: contraindicated
* Potential for drug-drug interactions with Paxlovid and CNI/mTOR’s
  + Ritonavir: very potent CYP3A4 inhibitor
    - Increases levels of CNIs and mTORs significantly
    - Majority of effect (mean 70-80%, 95% CI 10-92%) resolves within 48 hours of last dose.
    - Near complete resolution of effect (mean 95-96%, 95% CI 90-99%) within 7 days of last dose
* Recommended CNI/mTOR dosing modification while on concomitant Paxlovid are summarized in the table below

|  |  |  |  |
| --- | --- | --- | --- |
| **Days** | **Paxlovid** | **Tacrolimus or mTOR** | **Cyclosporine** |
| **1** | Take as prescribed twice daily for 5 days | HOLD therapy  (Days 1-7) | Continue therapy at an 80% reduced dose  (Days 1-7) |
| **2** |
| **3** |
| **4** |
| **5** |
| **6** | n/a |
| **7** | n/a |
| **8**  (48 hrs post Paxlovid) | n/a | Resume therapy at dose on prior to starting Paxlovid  (Day 8) | Resume therapy at dose on prior to starting Paxlovid  (Day 8) |
| *-* Obtain drug level as soon as possible to evaluate if adjustments warranted (ideally day 7-8 as just restarting therapy)  - Must consider patient specific factors such as: time post-transplant, rejection/infection history, other immunosuppression | |

* Frequent laboratory monitoring is warranted and should be prescribed even in the setting of COVID19
* Potential for drug-drug interactions with Paxlovid and other (non-immunosuppressant) drugs should also be evaluated prior to initiating therapy
  + Examples of some common drug interactions with Paxlovid include: atorvastatin, clopidogrel, nifedipine, rosuvastatin