

a. Desensitization

Transplant candidates should be considered for desensitization therapy when their cPRA \geq 80% or there is concern that finding an HLA compatible organ will not occur soon enough without desensitization. Desensitization strategies can be used in actively listed transplant patients or to facilitate transplant candidacy. Transplant candidacy may change based on results of desensitization.

Absolute Contraindications:

- Otherwise does not meet criteria for transplant
- Unacceptable HLA antibody profile based on consultation with HLA staff
- Documented adverse events to desensitization therapies

Relative Contraindications:

- Moderate-to-severe neuropathy at baseline
- ANC < 1000 in last 7 days
- Platelets < 100,000 in last 7 days
- Current or recent (< 14 days) severe systemic infection

Pre-transplant surveillance and retreatment criteria:

- Monthly HLA antibody testing required until transplant. Additional cycles of desensitization may be required at the discretion of the transplant team.

Time of Transplant and Post-transplant modifications:

- If virtual crossmatch is negative, preparedness for positive retrospective crossmatch is required.
- If virtual crossmatch is positive and transplant performed, initiate Positive Donor Crossmatch protocol at time of transplant

Phase 1 Desensitization – Outpatient

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| Day #1 | SQ Bortezomib 1.3 mg/m ² + IV Belatacept 10mg/kg |
| Day #4 | SQ Bortezomib 1.3 mg/m ² + IV Belatacept 10 mg/kg |
| Day #7 | SQ Bortezomib 1.3 mg/m ² |
| Day #10 | SQ Bortezomib 1.3 mg/m ² |
| Day # 14 | IV Belatacept 10mg/kg |
| Day # 28 | IV Belatacept 10mg/kg + HLA antibody surveillance |
| Day # 56 | IV Belatacept 10mg/kg |
| Day # 84 | IV Belatacept 10mg/kg |
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Phase 2 Desensitization - Inpatient

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| Day #1 | Plasmapheresis (1.5V) ⁽¹⁾ |
| Day #3 | Plasmapheresis (1.5V) + bortezomib (1.3 mg/m ²) + IV belatacept 10mg/kg |
| Day #5 | Plasmapheresis (1.5V) |
| Day #7 | Plasmapheresis (1.5V) + bortezomib (1.3 mg/m ²) + IV belatacept 10mg/kg |
| Day #8 | HLA Antibody Testing |
| Day #9 | Plasmapheresis (1.5 V) |
| Day #11 | Plasmapheresis (1.5 V) + bortezomib (1.3 mg/m ²) |
| Day #13 | Plasmapheresis (1.5 V) |
| Day #15 | HLA Testing → Plasmapheresis (1.5 V) + bortezomib (1.3 mg/m ²) + IVIg (1g/kg) ^(3,5) |
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| Day #29 | HLA Testing / TBNK Enumeration Panel |
| Day #43 | HLA Testing |

(1) Stop all ACEi/ARB/ARNI therapy 24-48 hrs prior to plasmapheresis

(2) Consider testing for active HBV and HCV prior to ritux

- Consider 2nd and 3rd cycles if not responding to therapy
- Consider replacing bortezomib with carfilzomib for refractory cases or significant side effects from bortezomib
- Monthly HLA antibody surveillance until time of transplant