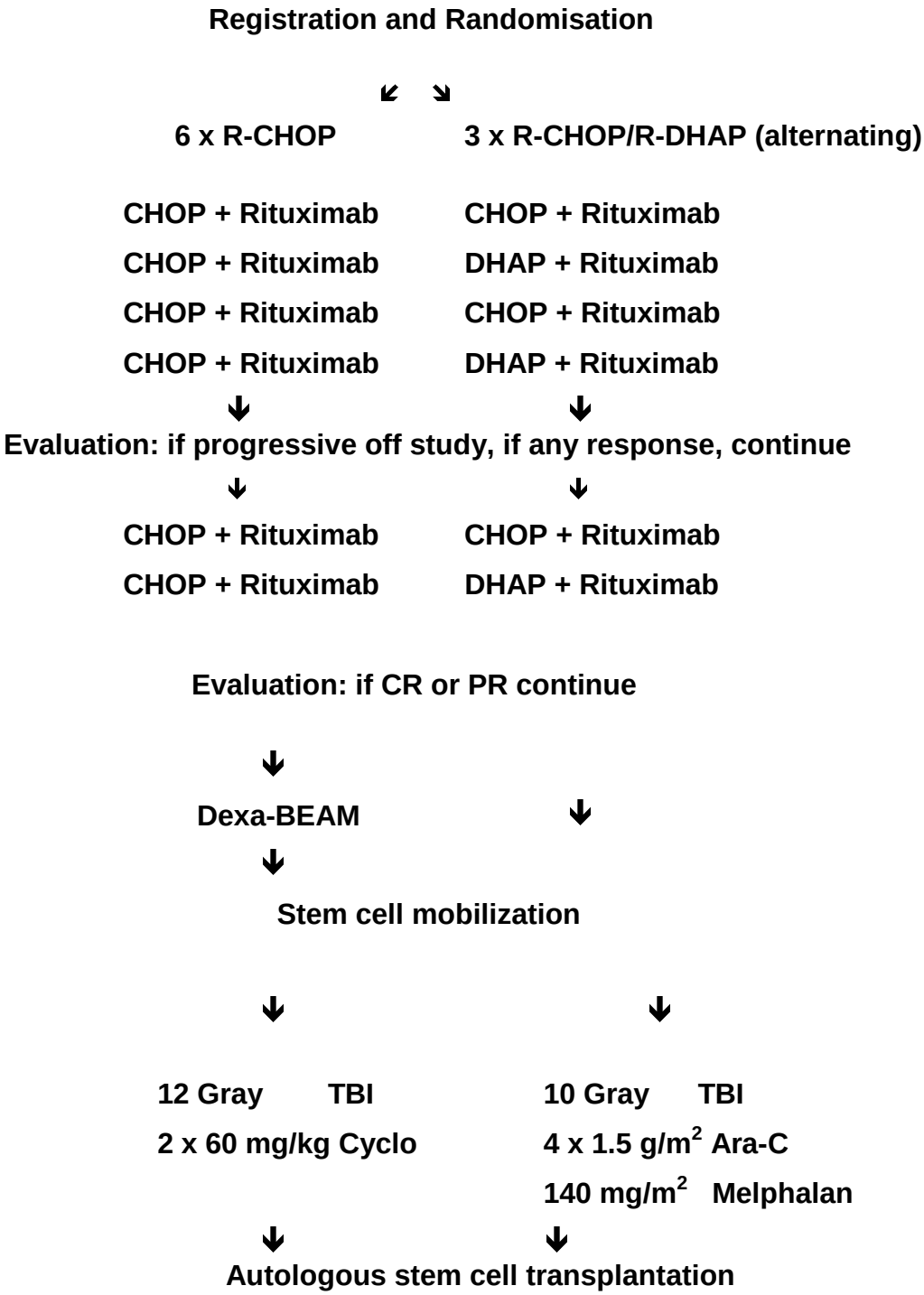1. TRIAL DESIGN