Hematopoietic stem cell transplantation is the only permanent treatment for the hematological manifestations in Fanconi anemia (FA). As FA patients have a dramatically increased intrinsic propensity to develop malignancies later in life and the genotoxic stress afflicted during conditioning advances the manifestation age especially of squamous cell carcinomas, choosing an optimally suited treatment regimen appears critical for long-term, tumor-free survival after stem cell transplantation. Here, we report our experiences in 6 consecutive FA patients transplanted with HLA-matched sibling donors where we combined an established pre-transplantation treatment consisting of thoraco-abdominal irradiation (TAI), cyclophosphamide (CYC) and cyclosporine A graft-versus-host prophylaxis with antibody-mediated IN VIVO T-cell depletion strategies after infusion of the graft. This approach has ensured sustained engraftment with long-term survival and an excellent post transplant performance status without any evidence of secondary malignancies in all six patients after a median follow-up of more than 10 years.