Supplementary Material

Table 2. Initial studies supporting approval of indications for sargramostim in hematopoietic recovery

Citation	Model	Disease Target	Study Design	Treatment	Treatment Adverse Events	Outcomes	Comments
Treatment of Delayed Neutrophil Recovery After Allogeneic or Autologous BMT							
Nemunaitis 1990 (1)	Allogeneic & autologous BMT	Hematologic (n=31) and solid (n=4) malignancy; aplastic anemia (n=2)	Phase 1-2 n = 192	BMT then: Sargramostim 60–1,000 µg/m^2/d IV over 2h x 14d/21d (n=37) vs Historic controls with graft failure (n=155)	*TRAE Sargramostim ≥500 µg/m^2/d (n = 4; 6 courses):* • n = 4, myalgias and bone pain during infusion *TRAE Sargramostim ≤250 µg/m^2 (n = 33; 46 courses):* • n = 1, sternal/joint pain	*Sargramostim:* • ANC >500/µL (within 14d of the final course): 57% *Sargramostim vs historic control:* • OS prolonged with sargramostim (p = .001) • Infection-related death: 21% vs 59% (p = NR)	Improved survival with sargramostim; majority of patients with neutrophil recovery by day 14 along with resolution of fever and infection
Acceleration of Myeloid Reconstitution After Autologous BMT							
Nemunaitis 1991 (2) / Rabinowe 1993 (3)	Autologous BMT	Hematologic malignancy (N=128)	Phase 3; Multicenter; Randomized; Double-blind; Placebo-controlled	BMT then: Sargramostim 250 µg/m^2 IV over 2 hr daily x 21 d (n=65) vs Placebo (n=63)	No differences between groups	*Sargramostim vs placebo:* • Median time to ANC ≥500/µL: 19d vs 26d (p < .001) • Median time to ANC >1000/µL: 26d vs 33d (p = .009) • ANC >500/µL within 21d: 59% vs 32% (p < .002)	• Decreased time to ANC >500 and 1000/µL, IV antibiotic use, and hospital LOS with sargramostim • On follow-up (median of 36 month), no graft failure, no increased risk of leukemogenesis • Sargramostim treatment an independent predictor of accelerated neutrophil engraftment regardless of disease or number/type of prior therapies

Citation	Model	Disease Target	Study Design	Treatment	Treatment Adverse Events	Outcomes	Comments
Acceleration of Myeloid Reconstitution After Allogeneic BMT							
Nemunaitis 1995 (4)	Allogeneic BMT	Hematologic malignancy (n=102); aplastic anemia (n=7)	Phase 3; Multicenter; Randomized; Double-blind; Placebo-controlled	BMT then: Sargramostim 250 μg/m^2 IV over 4h d0-d20 (n=53) vs Placebo (n=56)	No differences between groups	*Sargramostim vs placebo:* • Median time to ANC ≥500/μL: 13d vs 17d (p = .0001) • Median time to ANC ≥1,000/μL: 14d vs 19d (p = .0001) • Median time to platelets ≥20,000/μL: 24d vs 26d (p = NS)	Decreased time to ANC ≥500 and 1000/μL, infection, bacteremia, mucositis, LOS with sargramostim
Reduced Time to Neutrophil Recovery and Fewer Infections After Acute Myeloid Leukemia Induction (≥55 years old)							
Rowe 1995 (5) / Rowe 1996 (6)	Chemotherapy induction	Hematologic malignancy (N=124)	Phase 3; Randomized; Double-blind; Placebo-controlled; Multicenter	Induction and consolidation chemotherapy[a] then: Sargramostim 250 μg/m^2 IV over 4 hr daily starting d11 of induction and consolidation until ANC ≥1,500 x3d or a maximum of 42d (n=62) vs Placebo (n=62)	Grade 3-4 hemorrhagic, hepatic and neurologic adverse events were reduced in the subjects given sargramostim	*Sargramostim vs placebo:* • Median time to ANC >500/μL: 13d vs 17d (p = .001) • Median time to ANC >1000/μL: 14d vs 21d (p = .001) • Median time to platelets >20,000/μL: 11d vs 12d (p = NS) • Median OS: 10.6 mo vs 4.8 mo (p = .048) • Death from infection: 6% vs 23% (p = .019) • Death from fungal infection (overall): 2% vs 19% (p = .006) • Death from fungal infection (grade 3/4): 13% vs 75% (p = .02) • Death related to pneumonia: 14% vs 54% (p = .046)	• Sargramostim used in patients with *de novo* AML (age 55-70 yr) decreased time to ANC >500 and 1000/μL, reduced infections, death from infection, death from fungal infection, death from pneumonias • Increased OS with sargramostim

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Increased Survival in Hematopoietic Acute Radiation Syndrome							
Clayton 2021 (7)	Nonhuman primate	Myeloablation (N=108)	Randomized; Double-blind; Placebo-controlled	$LD_{50\text{-}60/60}$ TBI or $LD_{70\text{-}80//60}$ TBI Starting 48h post irradiation (without blood transfusions or individualized antibiotics): Sargramostim 7 µg/kg/d SC (~250 µg/m^2/d) vs vehicle SC daily until ANC >1,000/µL x 3d or ANC ≥10,000/µL	Not reported	*Sargramostim vs vehicle:* • Survival (day 60): ○ $LD_{50\text{-}60/60}$: 78% vs 42% (p = .0018) ○ $LD_{70\text{-}80//60}$: 61% vs 17% (p = .0076) • Infections: ○ $LD_{50\text{-}60/60}$: 32% vs 63% (p = .0001) ○ $LD_{70\text{-}80//60}$: 37% vs 84% (p < .0001)	Increased survival with sargramostim in the absence of intensive supportive care

[a]Induction with daunorubicin d1-3, cytarabine d1-7 x 2 (maximum) cycles plus consolidation with cytarabine

Abbreviations: AML, acute myeloid leukemia; ANC, absolute neutrophil count; BMT, bone marrow transplantation; IV, intravenous; $LD_{50\text{-}60/60}$, dose lethal in 50-60% by D60; $LD_{70\text{-}80/60}$, dose lethal in 70-80% by D60; LOS, length of stay; NR, not reported; NS, non-significant; OS, overall survival; SC, subcutaneously; TBI, total body irradiation; TRAE, treatment-related adverse event.

Supplementary References

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