ASCO® Guidelines

White Blood Cell Growth Factors: ASCO Guideline Update Supplement

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Data Supplement 1: Evidence Tables

Q1. Among adults treated with systemic antineoplastic therapy for a solid tumor or lymphoma, what factors should clinicians consider when selecting patients for primary prophylaxis of febrile neutropenia with a CSF?

Study characteristics

Author, year	Study type	Cancer details	Intervention/comparison	Age intervention/comparison (years)	% Female, intervention/comparison	Number randomized, intervention/comparison
Efficacy, G-CSF vs no G-CSF						
Fernandes 2018[1]	Systematic review	Early-stage breast cancer treated with six to eight cycles of FEC-D chemotherapy every 3 weeks	G-CSF or antibiotics vs No primary prophylaxis of FN	54	NR	11 studies, 1543 patients
Lyman 2018[2]	Meta-analysis	Solid tumors or malignant lymphoma treated with conventional-dose chemotherapy	Primary G-CSF vs No initial G-CSF	NR	NR	16 studies in group 1 (same antineoplastic therapy)
Glaspy 2023[3]	RCT	Stage II–IV breast cancer in the adjuvant or metastatic setting, treated with TA regimen (75 mg/m^2 docetaxel + 60 mg/m^2 doxorubicin)	Efbemalenograstim alfa vs Placebo	51 vs 52	100 vs 100	83 vs 39
Sun 2022[4]	RCT	NSCLC treated with multiple cycles of adjuvant chemotherapy, and including	Primary PEG-rhG-CSF vs control. Control arm received rhG-CSF if	59 vs 60	38 vs 40	94 vs 54

		a platinum-containing two-drug program (Intermediate or low risk of FN)	low white blood cell count or low absolute neutrophil count			
Pinter 2017[5]	RCT	Advanced colorectal cancer treated with bevacizumab plus first-line chemotherapy (FOLFOX [leucovorin, 5-fluorouracil, oxaliplatin] or FOLFIRI [leucovorin, 5-fluorouracil, irinotecan])	Pegfilgrastim vs Placebo	61 vs 61	41.2 vs 37.6	422 vs 423
Kosaka 2015[6]	RCT	Stage I-III breast cancer treated with docetaxel and cyclophosphamide (TC)	Pegfilgrastim vs Placebo	51 vs 50	100 vs 100	177 vs 174
Other questions						
Van Belle 2021[7]	Meta-analysis FN incidence without prophylaxis	Breast cancer treated with (neo)adjuvant docetaxel, carboplatin and trastuzumab, with or without pertuzumab (TCH(P))	No G-CSF	NR	NR	9 studies, n = 889 Primarily retrospective
Hoshina 2021[8]	Systematic review Of AE	Cancer and G-CSF-associated aortitis	All had received G-CSF	60.1	91.8	25 articles
Lapidari 2021[9]	Systematic review Of AE	Cancer treated with chemotherapy	Prophylactic G-CSF (primary or secondary) vs No prophylactic G-CSF	NR	NR	88 studies of any type
Chambers 2019[10]	Meta-analysis	Adults receiving chemotherapy	Patient characteristics	NR	NR	37 studies included in systematic

	Patient characteristics in relation to FN					review, 12 included in meta-analysis.
Truong 2016[11]	Meta-analysis Incidence of FN in RCTs vs observational studies	Breast cancer treated with chemotherapy. Each chemotherapy regimen had at least one nonrandomized prospective or retrospective cohort study and one RCT reporting FN rates.	RCT incidence of FN vs Observational cohort incidence of FN	52 vs 54	NR	RCT: 42,257 Observational: 7,812
Hershman 2023[12]	RCT Different approaches to patients with intermediate risk of FN	Breast, colorectal, or NSCLC with an intermediate risk of FN (10-20%). First-line therapy.	Secondary randomization for substudy in patients with intermediate risk of FN Standard order entry (SOE) to prescribe PP-CSF vs Alert not to prescribe PP-CSF	59 vs 59	60 vs 59	542 (12 sites) vs 304 (12 sites) (analysis groups)
Clemons 2021[13]	RCT Antibiotics vs G-CSF	Early breast cancer treated with docetaxel-cyclophosphamide (TC) chemotherapy	Antibiotics vs G-CSF	59 vs 57	NR	228 vs 230
Kirshner 2018[14]	RCT Bone pain prevention	Newly diagnosed stage I-III breast cancer treated with chemotherapy with pegfilgrastim support	Naproxen 500 mg BID vs Loratadine 10 mg QD vs No treatment For prevention of bone pain	53 vs 55 vs 55	100 vs 100 vs 100	200 vs 202 vs 198

Study results

Author, year	Study type	Cancer details	Intervention/comparison	Primary outcome	Efficacy results	Adverse events
Efficacy, G-CSF vs no G-CSF						
Fernandes 2018[1]	Systematic review	Early-stage breast cancer treated with six to eight cycles of FEC-D chemotherapy every 3 weeks	G-CSF or antibiotics vs No primary prophylaxis of FN	Incidence of FN	Risk of FN With primary prophylaxis: 10.1% Without primary prophylaxis: 23.9% (median values among the 11 included studies; no meta-analysis conducted)	Few studies provided information
Lyman 2018[2]	Meta-analysis Of RCTs	Solid tumors or malignant lymphoma treated with conventional-dose chemotherapy	Primary G-CSF vs No initial G-CSF	Delivered dose intensity, mortality, and secondary malignancy	Group 1 (same antineoplastic regimens) Mortality RR 0.97, 95% CI 0.93 to 1.01 16 studies	Secondary malignancies (not restricted to studies of patients who received same antineoplastic regimens) RR 1.85, 95% CI 1.19 to 2.88
Glaspy 2023[3]	RCT	Stage II–IV breast cancer in the adjuvant or metastatic setting, treated with TA regimen (75 mg/m^2	Efbemalenograstim alfa vs Placebo	Duration of severe (grade 4) neutropenia in cycle 1	Mean DSN in cycle 1 (days): 1.3 vs 3.9 Mean difference: 2.9 days (95% CI, 2.3 to 3.4)	Grade 3/4 AEs (%) Neutropenia: 60.3 vs 64.1 Leukopenia: 33.7 vs 35.9 Alopecia: 4.8 vs 2.6

		docetaxel + 60 mg/m^2 doxorubicin)				Diarrhea: 1.2 vs 2.6 Anemia, asthenia, thrombocytopenia (same results for each): 1.2 vs 0 Febrile neutropenia: 4.8 vs 25.7
Sun 2022[4]	RCT	NSCLC treated with multiple cycles of adjuvant chemotherapy, and including a platinum-containing two-drug program (Intermediate or low risk of FN)	Primary PEG-rhG-CSF vs control. Control arm received rhG-CSF if low white blood cell count or low absolute neutrophil count	Grade 3/4 neutropenia 130 of 148 included in "full analysis set."	Grade 3/4 neutropenia 1.15% vs 11.63% *P* < .05	Grade 3/4 AEs (n) 4 vs 11
Pinter 2017[5]	RCT	Advanced colorectal cancer treated with bevacizumab plus first-line chemotherapy (FOLFOX [leucovorin, 5-fluorouracil, oxaliplatin] or FOLFIRI [leucovorin, 5-fluorouracil, irinotecan])	Pegfilgrastim vs Placebo	Grade 3/4 FN in the first 4 cycles. Primary analysis included 783 patients who completed 4 treatment cycles.	Grade 3/4 FN: 2.4% vs 5.7%; OR 0.41, *P* = .014	Any grade 3 or worse 27.4% vs 28.3%

Kosaka 2015[6]	RCT	Stage I-III breast cancer treated with docetaxel and cyclophosphamide (TC)	Pegfilgrastim vs Placebo	FN	Incidence of FN 1.2% vs 68.8% *P* < 0.001	Bone pain 19.1% vs 15.0% Pyrexia and increased blood lactate dehydrogenase levels were also more common in pegfilgrastim arm
Other questions						
Van Belle 2021[7]	Meta-analysis FN incidence without prophylaxis	Breast cancer treated with (neo)adjuvant docetaxel, carboplatin and trastuzumab, with or without pertuzumab (TCH(P))	No G-CSF	Incidence of FN without G-CSF	FN incidence without G-CSF 27.4%, 95% CI, 18.6 to 37.1 9 studies, n = 889 Higher than in initial clinical trials	NR
Hoshina 2021[8]	Systematic review of AE	Cancer and G-CSF-associated aortitis	All had received G-CSF	G-CSF-associated aortitis	Not applicable	49 cases identified
Lapidari 2021[9]	Systematic review of AE	Cancer treated with chemotherapy	Prophylactic G-CSF (primary or secondary) vs No prophylactic G-CSF	Short- and long-term side effects of G-CSF	NR	Bone pain Most commonly reported AE. Incidence varies, but estimated at 25-38%

						Tends to be mild or moderate Does not appear to be affected by type of G-CSF Secondary malignancies Hard to draw definitive conclusions Quality of life Few studies, and mixed results
Chambers 2019[10]	Meta-analysis Of patient characteristics and FN	Adults receiving chemotherapy	Patient characteristics	Any neutropenic event (NE), i.e. FN, FN admission, dose delays due to neutropenia, or laboratory-tested myelosuppression.	Neutropenic event Increasing age: OR 1.39 (95% CI, 1.11 to 1.76), 4814 patients One co-morbidity vs none: OR 1.54 (95% CI, 1.09 to 2.19), 9189 patients	NR
Truong 2016[11]	Meta-analysis Of FN incidence in RCT vs observational studies	Breast cancer treated with chemotherapy. Each chemotherapy regimen had at least one nonrandomized prospective or retrospective	RCT incidence of FN vs Observational cohort incidence of FN	Incidence of FN	FN incidence, observational vs RCT Adjusted OR 1.74; 95% CI, 1.15 to 2.62 A 13% FN rate in an RCT would translate into 20% FN rate in an observational study	NR

		cohort study and one RCT reporting FN rates.				
Chambers 2019[10]	Meta-analysis Of patient characteristics and FN	Adults receiving chemotherapy	Patient characteristics	Any neutropenic event (NE), i.e. FN, FN admission, dose delays due to neutropenia, or laboratory-tested myelosuppression.	Neutropenic event Increasing age: OR 1.39 (95% CI, 1.11 to 1.76), 4814 patients One co-morbidity vs none: OR 1.54 (95% CI, 1.09 to 2.19), 9189 patients	NR
Hershman 2023[12]	RCT Different approaches to patients with intermediate risk of FN	Breast, colorectal, or NSCLC with an intermediate risk of FN (10-20%). First-line therapy.	Secondary randomization for substudy in patients with intermediate risk of FN Standard entry order (SOE) to prescribe PP-CSF vs Alert not to prescribe PP-CSF	Febrile neutropenia	Receipt of PP-CSF 37.1% vs 9.9% FN 3.7% vs 3.7%	NR (other than FN)
Clemons 2021[13]	RCT Antibiotics vs G-CSF	Early breast cancer treated with docetaxel-cyclophosphamide (TC) chemotherapy	Antibiotics vs G-CSF	Composite of FN and non-FN treatment-related hospitalization	Risk difference = -6.7%, 95% CI, -13.5% to 0.1% (risk of FN was lower in G-CSF arm)	Any primary or secondary endpoint (FN or treatment-related hospitalization, chemotherapy dose reduction, delay, or discontinuation, or

						microinjection) Risk difference -10.8%, 95% CI -19.7 to -1.9
Kirshner 2018[14]	RCT Bone pain prevention	Newly diagnosed stage I-III breast cancer treated with chemotherapy with pegfilgrastim support	Naproxen 500 mg BID vs Loratadine 10 mg QD vs No treatment For prevention of bone pain	All-grade bone pain in cycle 1, from AE reporting	All-grade bone pain Naproxen: 40.3% Loratadine: 42.5% No treatment: 46.6% *P* > 0.05	Grade 3 or greater treatment-related AEs Naproxen: 1% Loratadine: 0 Treatment-related AEs leading to discontinuation of naproxen or loratadine Naproxen: 4.7% Loratadine: 0

Q2. Among adults treated with systemic antineoplastic therapy for a solid tumor or lymphoma, what factors should clinicians use to select patients for secondary prophylaxis of febrile neutropenia with a CSF?

Study characteristics

Author, year	Study type	Cancer details	Intervention/comparison	Age intervention/comparison (years)	% Female, intervention/comparison	Number randomized, intervention/comparison
Leonard 2015[15]	RCT	Breast cancer treated with adjuvant or neoadjuvant chemotherapy, with a first neutropenic event	G-CSF vs Standard management (dose delay or dose reduction)	NR	100 vs 100	204 vs 203

Study Results

Author, year	Intervention/comparison	Primary outcome	Efficacy results	Adverse events	Note
Leonard 2015[15]	G-CSF vs Standard management (dose delay or dose reduction)	Receiving planned dose intensity	85% planned relative dose intensity (RDI) 75% vs 50% *P* < .0001	Only provided rates for category or grade 2 or greater. Did not comment on grade 3 or greater.	Trial size was amended from 816 to 407, due to difficulty in recruitment.

Q3. Are there circumstances in which CSFs should be considered for the treatment of neutropenia among adults with cancer?

No new studies identified.

Q4. What is the role of CSFs as adjuncts to progenitor-cell transplantation?

Study characteristics

Author, year	Study type	Cancer details	Intervention/comparison	Age intervention/comparison (years)	% Female, intervention/comparison	Number randomized, intervention/comparison
Mobilization						
Li 2024[16]	Meta-analysis	Patients with multiple myeloma, non-Hodgkin's lymphoma, and Hodgkin's lymphoma undergoing autologous hematopoietic stem cell transplantation	G-CSF plus plerixafor G-CSF	NR	NR	23 studies, single- or multicenter, prospective, or retrospective
Luo 2022[17]	Meta-analysis Network, of RCTs	Primary diagnosis of hematologic malignancy and eligible for autologous hematopoietic stem cell transplantation. Meta-analysis results provided for multiple myeloma and NHL.	Multiple myeloma comparisons G-CSF SD versus -G-CSF SD plus plerixafor SD -ID-AraC plus G-CSF SD -CY plus G-CSF RD -Pegfilgrastim (12 mg or 18 mg) NHL comparisons G-CSF SD versus -G-CSF SD plus plerixafor SD -G-CSF SD plus YF-H-2015005	Overall NR	Overall NR	Network meta-analysis: 13 RCTs, n=638 with multiple myeloma and n=592 with NHL

Wang 2021[18]	Meta-analysis	Multiple myeloma and autologous stem cell transplantation	Cyclophosphamide plus G-CSF vs G-CSF alone The most common dose of G-CSF was 10 µg/kg with filgrastim or lenograstim	Overall NR	Overall NR	4 prospective and 14 retrospective studies (n= 2770 patients)
Goto 2025[19]	RCT Phase II	Multiple myeloma	Pegfilgrastim vs filgrastim	30 vs 30	37 vs 37	59 vs 60
Jeker 2024[20]	RCT Phase II noninferiority	Multiple myeloma	Chemotherapy plus G-CSF vs G-CSF	62 vs 63	35 vs 49	68 vs 68
Crees 2023[21]	RCT	Multiple myeloma	G-CSF plus motixafortide vs G-CSF plus placebo	64 vs 62	31.2 vs 42.9	80 vs 42
G-CSF after autologous HSCT						
Grosso 2022[22]	RCT	Patients with multiple myeloma or non-Hodgkin lymphoma who underwent pegfilgrastim plus plerixafor-primed stem cell collection followed by autologous hematopoietic stem cell transplantation	G-CSF starting 3 days after transplant vs No G-CSF after transplant	61 vs 65	31 vs 51	35 vs 35
G-CSF after allogeneic HSCT						
Wan 2015[23]	RCT Phase IV	Allogeneic hematopoietic stem-cell transplantation	GM-CSF vs GM-CSF plus G-CSF vs G-CSF	31 vs 33 vs 32	25 vs 46.4 vs 36.2	68 vs 69 vs 69

Study results

Author, year	Study type	Intervention/comparison	Number randomized, intervention/comparison	Primary outcome	Efficacy results	Adverse events
Mobilization						
Li 2024[16]	Meta-analysis	G-CSF plus plerixafor G-CSF	23 studies, single- or multicenter, prospective, or retrospective	CD34+ cells	Achieved predetermined yield of CD34+ cells 64.9% vs 33.8% *P* < .00001 12 studies, n=2137	Grade of AEs NR TEAEs G-CSF + plerixafor: 78.4%, G-CSF: 80.1%, *P* = 0.23 8 studies, n=986
Luo 2022[17]	Meta-analysis Network, of RCTs	Multiple myeloma comparisons G-CSF SD versus -G-CSF SD plus plerixafor SD -ID-AraC plus G-CSF SD -CY plus G-CSF RD -Pegfilgrastim (12 mg or 18 mg) NHL comparisons G-CSF SD versus	Network meta-analysis: 13 RCTs, n=638 with multiple myeloma and n=592 with NHL	Total number of collected CD34+ cells (× 10^6/kg)	Relative to G-CSF SD Multiple myeloma -G-CSF SD plus plerixafor SD: MD 4.15, 95% CrI, 2.92 to 5.39 ID-AraC plus G-CSF SD: MD 14.29, 95% CrI, 9.99 to 18.53 -CY plus G-CSF RD: MD 1.18, 95% CrI, 0.29 to 2.07 -Pegfilgrastim 12 mg: MD -1.46, 95% CrI, -2.63 to -0.28 -Pegfilgrastim 18 mg: MD -1.86, 95% CrI, -3.57 to -0.15 8 trials	NR

		-G-CSF SD plus plerixafor SD -G-CSF SD plus YF-H-2015005			NHL -G-CSF SD plus plerixafor SD: MD 3.62, 95% CrI, 2.86 to 4.38 -G-CSF SD plus YF-H-2015005: MD 3.43, 95% CrI, 2.51 to 4.35	
Wang 2021[18]	Meta-analysis	Cyclophosphamide plus G-CSF vs G-CSF alone The most common dose of G-CSF was 10 µg/kg with filgrastim or lenograstim.	4 prospective and 14 retrospective studies (n= 2770 patients)	Efficiency, safety of mobilization, and survival outcomes after autologous hematopoietic stem cell transplantation	Yield of CD34+ cells SMD=0.45, 95% CI 0.24 to 0.66 Successful mobilization rate OR=2.8, 95% CI, 1.82 to 4.29 Response after ASCT of very good partial response or better OR= 0.59, 95% CI, 0.39 to 0.90 EFS HR 0.73,95% CI, 0.58 to 0.93 No significant difference in OS, PFS	Risk of admission OR=26.49, 95% CI 7.31 to 95.97 Fever OR=13.66, 95% CI 6.21 to 30.03
Goto 2025[19]	RCT Phase II	Pegfilgrastim vs filgrastim	30 vs 30	≥2 X 10^6/kg CD34-positive cells collected during the	100% vs 96.7%	One grade 3 or greater TEAE (hypocalcemia) occurred in pegfilgrastim arm

				whole apheresis period		
Jeker 2024[20]	RCT Phase II noninferiority	Chemotherapy plus G-CSF vs G-CSF	68 vs 68	Successful stem cell mobilization (≥ 5.0 X 10^6 CD34+ cells/kg body weight in a single day collection procedure without additional stimulation with plerixafor)	78% vs 60% Difference was outside of the 15% non-inferiority margin	Frequency of severe AEs related to mobilization treatment was similar between study arms
Crees 2023[21]	RCT Phase III	G-CSF plus motixafortide vs G-CSF plus placebo	80 vs 42	Proportion of patients collecting ≥6 × 10^6 CD34(+) cells kg^{-1} within two apheresis procedures	Primary endpoint 92.5% vs 26.2% OR 53.3, 95% CI, 14.12 to 201.33	Grade 3 TEAEs (%) G-CSF plus motixafortide: 27.5 G-CSF plus placebo: 4.8 No grade 4 or 5
G-CSF after autologous HSCT						
Grosso 2022[22]	RCT	G-CSF starting 3 days after transplant vs No G-CSF after transplant	35 vs 35	Length of stay	LOS (days) 11 vs 15 *P* = .001 Study closed early for futility	G-CSF associated with fewer days of febrile neutropenia (*P* = .001), and fewer days on antibiotics (*P* = .001), NS differences in platelet recovery, documented infections, hospital readmissions, and overall survival at 1 year
G-CSF after allogeneic HSCT						

Wan 2015[23]	RCT Phase IV	GM-CSF vs GM-CSF plus G-CSF vs G-CSF	68 vs 69 vs 69	100-day incidence of proven and probable invasive fungal disease and response rate of antifungal treatment.	Proven and probable invasive fungal disease (%) 11.8 vs 10.1 vs 23.2 *P* = .07 Response to anti-fungal treatment *P* = .05 Planned power 70%	Grade 2 or greater acute GvHD 30.9% vs 24.6% v 21.7% P = .47 100-day mortality 10.3% vs 11.6% vs 24.6% P = .04

Q5. Should CSFs be avoided in patients receiving concomitant chemotherapy and radiation therapy?

Study characteristics

Author, year	Study type	Cancer details	Intervention/comparison	Age intervention/comparison (years)	% Female, intervention/comparison	Number randomized, intervention/comparison
Yang 2025[24]	RCT	Locally advanced nasopharyngeal cancer treated with chemoradiotherapy	PEG-rhG-CSF vs no PEG-rhG-CSF	51 vs 52	36% vs 27%	44 vs 44
Zou 2021[25]	RCT	Stage IIb-IIIb cervical squamous cell carcinoma treated chemoradiotherapy	PEG-rhG-CSF vs no PEG-rhG-CSF. If ANC < 1 X 10^9/L, 5 μg/kg/d rhG-CSF given	54 vs 54	100 vs 100	40 vs 18 No sample size calculations, industry-funded, stage differential between study arms (control arm had higher stage cancer)

Study results

Author	Study type	Intervention/comparison	Number randomized, intervention/comparison	Primary outcome	Efficacy results	Adverse events
Yang 2025[24]	RCT	no PEG-rhG-CSF	44 vs 44	Grade 3 or 4 neutropenia	Grade 3 neutropenia 0 vs 13.6% *P* = .03	Difference in platelet levels did not differ significantly between study arms.

		If low leukocyte or neutrophil count rhG-CSF given				Grade 3 or 4 oral mucositis 32% vs 50% *P* = .06 (no information about other grade 3 or 4 AEs)
Zou 2021[25]	RCT	PEG-rhG-CSF vs no PEG-rhG-CSF If ANC < 1 X 10^9/L, 5 μg/kg/d rhG-CSF given	40 vs 18	Grade 3-4 neutropenia	10% vs 78% *P* < .001	Grade of AEs not provided Decreased platelets: 1 (2.5%) vs 0

Q6. Do CSFs differ in efficacy or safety?

Study characteristics

Author, year	Study type	Cancer details	Intervention/comparison	Age intervention/comparison (years)	% Female, intervention/comparison	Number randomized, intervention/compar
Biosimilar versus reference biologic						
Na 2023[26]	Meta-analysis	RCTs in cancer with comparative safety outcomes between a biosimilar and the original biologic	Biosimilar filgrastim or pegfilgrastim vs Original biologic G-CSF	NR	NR	9 studies
Yang 2019[27]	Meta-analysis	Cancer	G-CSF biosimilars vs Reference biologics	Overall NR	Overall NR	13 RCTs and 10 cohort studies
Kowalyszyn 2022[28]	RCT noninferiority	Breast cancer stages II-IV, treated with chemotherapy	Pegfilgrastim biosimilar vs Pegfilgrastim	55 vs 57	100 vs 100	59 vs 62
Link 2021[29]	RCT noninferiority	Aggressive B cell non-Hodgkin lymphoma (NHL) treated with six cycles of R-CHOP21.	Lipegfilgrastim vs Pegfilgrastim	72 vs 75	56 vs 45	49 vs 50
Waller 2019[30]	RCT	Newly diagnosed stage II/III breast cancer eligible for treatment with (neo)adjuvant chemotherapy with docetaxel/doxorubicin/cyclophosphami	Pegfilgrastim-jmdb vs Pegfilgrastim	50 vs 50	99 vs 100	127 vs 67

		de every 3 weeks for 6 cycles				
Blackwell 2018[31]	RCT Phase III noninferiority	Breast cancer treated with (neo)adjuvant TAC (docetaxel + doxorubicin + cyclophosphamide)	Alternating filgrastim-sndz and filgrastim vs Filgrastim every cycle	49 vs 47	100 vs 100	110 vs 54
Eflapegrastim-xnst vs pegfilgrastim						
Schwartzberg 2020[32]	RCT noninferiority	Early-stage breast cancer treated with standard docetaxel plus cyclophosphamide chemotherapy for 4 cycles	Eflapegrastim-xnst vs Pegfilgrastim	61 vs 60	>99 vs >99	196 vs 210
Cobb 2020[33]	RCT noninferiority	Breast cancer stage I to IIIA treated with adjuvant or neoadjuvant standard docetaxel/cyclophosphamide (TC) chemotherapy	Eflapegrastim-xnst vs Pegfilgrastim	58 vs 59	100 vs 100	118 vs 119
Efbemalenograstim alfa vs pegfilgrastim, filgrastim, or placebo						
Glaspy 2024[34]	RCT Phase II	Stage I-IV invasive breast cancer. 141 patients treated with docetaxel + cyclophosphamide (TC) and	Efbemalenograstim alfa lower weight-based dose vs Efbemalenograstim alfa higher weight-	TAC population 48 vs 46 vs 48	100	TAC population 30 vs 31 vs 30

		91 patients treated with docetaxel + doxorubicin + cyclophosphamide (TAC). Enrollment was limited to TAC after interim analysis, due to low risk of severe neutropenia in TC arm.	based dose vs Pegfilgrastim Day 2			
Zhang 2024[35]	RCT	Breast cancer treated with up to four cycles of adjuvant epirubicin and cyclophosphamide (China)	Efbemalenograstim alfa, single 20 mg sc dose on day 3 vs Filgrastim, daily 5 mcg/kg/day sc dose starting on day 3	49.1 vs 48.5	100 vs 100	122 vs 120
Glaspy 2023[3]	RCT	Stage II–IV breast cancer in the adjuvant or metastatic setting, treated with TA regimen (75 mg/m^2 docetaxel + 60 mg/m^2 doxorubicin)	Efbemalenograstim alfa 20 mg vs Placebo	51 vs 52	100 vs 100	83 vs 39
PEGylated G-CSF vs G-CSF						
Wang 2021[36]	Meta-analysis	Cancer in adults treated with chemotherapy	Long-acting G-CSF vs Standard G-CSF	Overall NR	Overall NR	10 studies, 1916 patients

Li 2020[37]	Meta-analysis	Breast cancer	PEGylated G-CSF vs G-CSF	Overall NR	NR	9 RCTs
Wang 2019[38]	Meta-analysis	Patients with cancer treated with chemotherapy	Comparisons of 11 G-CSF drugs	Overall NR	Overall NR	73 RCTs, 15,124 patie
Cornes 2018[39]	Meta-analysis	Non-myeloid malignancies treated with myelosuppressive anticancer drugs or acute myeloid leukemia treated with induction or consolidation chemotherapy	Long-acting G-CSF vs Short-acting G-CSF For primary or secondary G-CSF prophylaxis or treatment	Overall NR	Overall NR	11 RCTs
Huang 2023[40]	RCT (neutropenia treatment)	Breast cancer and chemotherapy-induced grade 3–4 neutropenia or FN.	PEG-rhG-CSF vs rhG-CSF	49 vs 47	NR	50 vs 50
Li 2023[41]	RCT (among patients treated with concurrent chemo and RT)	Stage IB–IVA cervical cancer treated with concurrent chemoradiotherapy	PEG-rhG-CSF vs rhG-CSF	50 vs 50	NR	21 (79 chemotherapy 19 (72 chemotherapy
Ding 2022[42]	RCT	Newly diagnosed multiple myeloma (MM) treated with bortezomib, lenalidomide, and dexamethasone (VRd).	Long-acting G-CSF vs Standard G-CSF For primary prophylaxis	62 vs 65	45 vs 54	33 vs 35

Study Results

Author, year	Study type	Intervention/comparison	Number randomized, intervention/comparison	Primary outcome	Efficacy results	Adverse events
Biosimilar versus reference biologic						
Na 2023[26]	Meta-analysis	Biosimilar filgrastim or pegfilgrastim vs Original biologic G-CSF	9 studies	Safety	NR	Serious TEAE RR 0.92, 95% CI, 0.57 to 1.49 TEAE, leading to death RR 1.97, 95% CI, 0.64 to 6.05
Yang 2019[27]	Meta-analysis	G-CSF biosimilars vs Reference biologics	13 RCTs and 10 cohort studies	Incidence of febrile neutropenia (FN), duration of severe (grade 4) neutropenia (DSN), time to ANC recovery	Incidence of FN RR = 1.09; 95% CI, 0.80 to 1.49 8 RCTs, n=1919 DSN cycle 1 WMD 0.03, 95% CI, -0.07 to 0.13 8 RCTs, n=2159 Time to ANC recovery WMD 0.07, 95% CI, -0.10 to 0.24 5 RCTs, n=1295 Subgroup analyses: no significant	Bone pain RCT RR 0.90, 95% CI, 0.78 to 1.05 4 RCTs, n=1212

					heterogeneity in type of G-CSF biosimilar (filgrastim biosimilars vs pegfilgrastim biosimilars) or type of tumor ($P > 0.05$)	
Kowalyszyn 2022[28]	RCT noninferiority	Pegfilgrastim biosimilar vs Pegfilgrastim	59 vs 62	Duration of severe neutropenia (DSN) in cycle 1	DSN Mean ± standard deviation (days), ITT population 0.90 ± 1.79 vs 0.50 ± 1.21 Noninferior	Serious adverse events (n of patients) 3 vs 5 Grades of adverse drug reactions NR
Link 2021[29]	RCT noninferiority	Lipegfilgrastim vs Pegfilgrastim	49 vs 50	Duration of severe neutropenia (DSN) in cycle 1	Adjusted mean difference in DSN (days), ITT population -0.1, 95% CI, -0.56 to 0.30	Serious AEs 46% vs 46% Withdrew from study due to AEs 2% vs 18%
Waller 2019[30]	RCT	Pegfilgrastim-jmdb vs Pegfilgrastim	127 vs 67	Duration of severe neutropenia in cycle 1	Mean (standard deviation) 1.2 days (0.93) vs 1.2 days (1.10)	TEAE grade ≥4 (n) 1 (grade 4 FN) vs 0
Blackwell 2018[31]	RCT Phase III noninferiority	Alternating filgrastim-sndz and filgrastim vs Filgrastim every cycle	110 vs 54	Febrile neutropenia incidence	3.4% vs 0% Met criteria for non-inferiority	Serious TEAEs 4.7% vs 2% Grade 3/4 TEAEs 18.7% vs 17.6%

Eflapegrastim-xnst vs pegfilgrastim						
Schwartzberg 2020[32]	RCT noninferiority	Eflapegrastim-xnst vs Pegfilgrastim	196 vs 210	Duration of severe neutropenia (DSN) in cycle 1	DSN, cycle 1 (days) MD -0.15, 95% CI, -0.26 to -0.03 Noninferiority *P* < .0001	Grade 3 AEs 18% vs 11%
Cobb 2020[33]	RCT noninferiority	Eflapegrastim-xnst vs Pegfilgrastim	118 vs 119	Duration of severe neutropenia (DSN) in cycle 1	DSN cycle 1 (days) MD -0.07, 95% CI, -0.29 to 0.13 Noninferiority *P* < .0001	Grade 3/4 AEs 14% vs 7% Serious AEs 10% vs 16%
Efbemalenograstim alfa vs pegfilgrastim, filgrastim, or placebo						
Glaspy 2024[34]	RCT Phase II	Efbemalenograstim alfa lower weight-based dose vs Efbemalenograstim alfa higher weight-based dose vs Pegfilgrastim Day 2	TAC population 30 vs 31 vs 30	Duration of moderate and severe neutropenia during cycle 1 (days)	TAC population Mean (standard deviation) 2.1 (1.58) vs 2.1 (1.46) vs 1.8 (1.28) Efbemalenograstim alfa was non-inferior to pegfilgrastim	Serious adverse events 1.5% vs 1.5% vs 6.2%
Zhang 2024[35]	RCT	Efbemalenograstim alfa, single 20 mg sc dose on day 3 vs Filgrastim, daily 5 mcg/kg/day sc dose starting on day 3	122 vs 120	Duration of grade 3 or 4 neutropenia in cycle 1	Duration of grade 3 or 4 neutropenia in cycle 1, mean ± standard deviation (days) 0.68 ± 1.10 vs 0.71 ± 0.95 (Efbemalenograstim alfa non-inferior)	Serious AEs (% of patients) 5.0 vs 6.7

Glaspy 2023[3]	RCT	Efbemalenograstim alfa 20 mg vs Placebo	83 vs 39	Duration of severe (grade 4) neutropenia in cycle 1	Mean DSN in cycle 1 (days): 1.3 vs 3.9 Mean difference: 2.9 days (95% CI 2.3 to 3.4)	Grade 3/4 AEs (%) Neutropenia: 60.3 vs 64.1 Leukopenia: 33.7 vs 35.9 Alopecia: 4.8 vs 2.6 Diarrhea: 1.2 vs 2.6 Anemia, asthenia, thrombocytopenia (same results for each): 1.2 vs 0 Febrile neutropenia: 4.8 vs 25.7
PEGylated G-CSF vs G-CSF						
Wang 2021[36]	Meta-analysis	Long-acting G-CSF standard G-CSF	Ten studies, 1916 patients	Incidence of febrile neutropenia or grade 3 or higher neutropenia, duration of severe neutropenia (DSN) time to absolute neutrophil count (ANC) recovery	Febrile neutropenia incidence RR 0.82, 95% CI, 0.57 to 1.17 Severe neutropenia incidence RR 0.86, 95% CI, 0.76 to 0.96 Duration of severe neutropenia MD -0.19, 95% CI, -0.38 to 0.00 Time to ANC recovery	Incidence of bone/muscle pain RR 0.75, 95% CI, 0.58 to 0.98 Incidence of fatigue RR 0.82, 95% CI, 0.62 to 1.07

					MD -0.23, 95% CI, -0.49 to 0.03	
Li 2020[37]	Meta-analysis	PEGylated G-CSF vs G-CSF	9 RCTs	Incidence and duration of grade ≥3 neutropenia in cycle 1	Grade ≥ 3 neutropenia RR=0.87, 95% CI, 0.69 to 1.1 Duration of grade ≥ 3 neutropenia WMD = -1.04, 95% CI, -2.30 to 0.23	Grade 4 AEs RR = 0.82, 95% CI, 0.57 to 1.18 Skeletal or muscle pain RR = 0.77, 95% CI, 0.46 to 1.29
Wang 2019[38]	Meta-analysis	Comparisons of 11 G-CSF drugs	73 RCTs, 15,124 patients	Febrile neutropenia, severe neutropenia, bone pain	Filgrastim vs pegfilgrastim, from direct pairwise meta-analysis Febrile neutropenia: OR 1.46, 95% CI, 1.07 to 1.99 16 trials, n=3399 Severe neutropenia OR 1.07, 95% CI, 0.90 to 1.27 12 trials, n=2860	Filgrastim vs pegfilgrastim, from direct pairwise meta-analysis Bone pain OR 1.40, 95% CI, 0.81 to 2.40 11 trials, n=1843
Cornes 2018[39]	Meta-analysis	Long-acting G-CSF vs Short-acting G-CSF For primary or secondary G-CSF prophylaxis or treatment	11 RCTs	Febrile neutropenia	Febrile neutropenia RR = 0.86, 95% CI, 0.68 to 1.10, *P* = 0.23 11 RCTs	NR

Huang 2023[40]	RCT (neutropenia treatment)	PEG-rhG-CSF vs rhG-CSF	50 vs 50	Duration of grades 3 and 4 neutropenia following the first cycle of chemotherapy.	Recovery time (days) 2.37±1.09 vs 3.89±1.46 *P* = 0.000	No grade 3 or worse AEs
Li 2023[41]	RCT (among patients treated with concurrent chemo and RT)	PEG-rhG-CSF vs rhG-CSF	21 (79 chemotherapy cycles) 19 (72 chemotherapy cycles)	Incidence of grade 3–4 neutropenia	Grade 3/4 neutropenia 0 vs 5.56% of cycles *P* = 0.046	Grade 3/4 (%) Decreased WBC count: 38.1 vs 63.2 Decreased platelet count: 9.5 vs 5.3 Anemia: 28.6 vs 26.3
Ding 2022[42]	RCT	Long-acting G-CSF vs Standard G-CSF For primary prophylaxis	33 vs 35	Incidence of febrile neutropenia, early infection (during the first 4 months of treatment), and treatment delays.	Incidence of febrile neutropenia: 6.1% vs 17.1% *P* = 0.30 Early infection: 6.1% vs 25.7% *P* = 0.03 Treatment delay: 9.1% vs 31.4% *P* = 0.03	No grade 4 thrombocytopenia

Q7. What are recommendations for the initiation, duration, dosing, and administration of CSFs?

Study characteristics

Author, year	Study type	Cancer details	Intervention/ comparison	Age intervention/ comparison (years)	% Female, intervention/ comparison	Number randomized, intervention/ comparison
Dose of pegfilgrastim						
Yang 2024[43]	RCT Non-inferiority	Stage IA to IIIC breast cancer treated with epirubicin (or pirarubicin) and cyclophosphamide	PEG-rhG-CSF 3 mg vs 6 mg, with stratification by body weight (≤60 kg vs > 60 kg)	45.5 vs 48.5	100 vs 100	62 vs 60
Ji 2022[44]	RCT	Stage IIIB/IVA lung cancer (NSCLC or SCLC) treated with chemotherapy	3 mg dose of PEG rhG-CSF vs No PEG rhG-CSF	62 vs 62	37 vs 39	230 vs 232
Masuda, 2015[45]	RCT Phase II, dose-finding	Stage II or III primary invasive breast carcinoma	1.8 mg pegfilgrastim vs 3.6 mg pegfilgrastim vs 6.0 mg pegfilgrastim	46 vs 47 vs 48	100 vs 100 vs 100	30 vs 30 vs 30
Timing of pegfilgrastim						
Xu 2024[46]	RCT	Early breast cancer	Pegfilgrastim on day 7 vs day 3 after chemotherapy	48 vs 50	NR	80 vs 80
Duration of filgrastim						

Clemons 2020[47] Duration of filgrastim	RCT	Early breast cancer	5 days filgrastim vs 7 or 10 days filgrastim	56 vs 56	NR	184 vs 282
Bozzoli 2015[48] Duration of filgrastim	RCT	Older adults with. previously untreated diffuse large B-cell lymphoma treated with R-CHOP-14 (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone given every 14 days)	Four doses of filgrastim from day +8 to +11 per cycle vs Pegfilgrastim once per cycle	66 vs 67	62 vs 59	24 vs 27
Timing of filgrastim						
Kim 2025[49]	RCT	Patients with breast cancer receiving TAC chemotherapy	Filgrastim starting on day 2 vs day 5	48 vs 48	NR	30 vs 30

Study results

Author, year	Study type	Intervention/ comparison	Number randomized, intervention/ comparison	Primary outcome	Efficacy results	Adverse events
Dose of pegfilgrastim						
Yang 2024[43]	RCT non-inferiority	PEG-rhG-CSF 3 mg vs 6 mg, with stratification by	62 vs 60	Timely ANC recovery before second cycle	Overall 89.8% vs 93.0% One-sided 95% CI lower limit of	Grade 3 or higher 35.0% vs 36.7% No grade 3 or higher

		body weight (≤60 kg vs > 60 kg)			difference: -11.7% Within non-inferiority margin of -15% ≤60 kg 93.3% vs 96.6% >60 kg 86.2% vs 89.3%	AEs were attributed to PEG-rhG-CSF
Ji 2022[44]	RCT	3 mg dose of PEG rhG-CSF vs No PEG rhG-CSF	230 vs 232	Incidence of acute lower respiratory tract infection, including pneumonia and bronchitis	Acute lower respiratory tract infection 9.6% vs 24.6% *P* < .01	AEs ≥ grade 3: 3 patients in PEG rhG-CSF group had back or lower limb pain.
Masuda, 2015[45]	RCT Phase II, dose-finding	1.8 mg pegfilgrastim vs 3.6 mg pegfilgrastim vs 6.0 mg pegfilgrastim	30 vs 30 vs 30	Duration of severe (grade 4) neutropenia in the first cycle (DSN).	DSN (days) 2.2 (±0.9) vs 1.5 (±0.9) vs 1.4 (±0.7)	Serious non-fatal AEs Four patients the 1.8-mg group (upper respiratory tract inflammation, cystitis, pneumonia, and radius fracture) and one patient in the 6.0-mg group (decreased appetite and malaise). Grade 3/4 hematologic AEs across groups Neutropenia: 97%-100%

						Leukocytopenia: 97%-100% Anemia: 0-3% Thrombocytopenia: 0-14% Lymphopenia: 38-45%
Timing of pegfilgrastim						
Xu 2024[46]	RCT	Pegfilgrastim on day 7 vs day 3 after chemotherapy	80 vs 80	Incidence of grade 3 or 4 neutropenia, FN	Grade 3 or 4 neutropenia 15.8% vs 29.9% *P* = .04 FN 4.0% vs 6.6% *P* = .72	No grade 3 or 4 AEs.
Duration of filgrastim						
Clemons 2020[47]	RCT	5 days filgrastim vs 7 or 10 days filgrastim	184 vs 282	Composite of either FN or treatment-related hospitalizations.	Composite of either FN or treatment-related hospitalizations 2.09% vs 3.60% RD -1.52%, 95% CI, -3.22% to 0.19%	Grade 3/4 NR
Bozzoli 2015[48]	RCT	Four doses of filgrastim from day +8 to +11 per cycle vs Pegfilgrastim once per cycle	24 vs 27	Dose intensity of R-CHOP-14	Median dose-intensity 87.5% vs 89.4% *P* = 0.9	Grade of AEs NR Febrile neutropenia (%): 21 vs 15, *P* = 0.3 Unplanned hospitalizations (%):

						13 vs 19, *P* = 0.7 Death during therapy (%): 4.2 vs 7.4, *P* = 1.0
Timing of filgrastim						
Kim 2025[49]	RCT	Filgrastim starting on day 2 vs day 5	30 vs 30	Incidence of FN	Incidence of FN for all cycles 6.4% vs 22.2% *P* < .0001	NR

Data Supplement 2: GRADE Summary Tables

Clinical Question 1: Primary Prophylaxis
PICO (1.1)
Population: People with cancer treated with chemotherapy
Intervention: Filgrastim
Comparator: Placebo

Outcome	Study results and measurements	Absolute effect estimates Placebo Filgrastim	Quality of evidence	Summary
Febrile neutropenia	Odds ratio: 0.49 (95% CI, 0.38 to 0.62) Based on data from 2460 participants in 16 studies[38]	**374** per 1000 **226** per 1000 Difference: **148 fewer per 1000** (95% CI, 189 fewer to 104 fewer)	**High**	Compared with placebo, filgrastim reduces the risk of febrile neutropenia.
Bone pain	Odds ratio: 2.07 (95% CI, 1.08 to 3.97) Based on data from 1673 participants in 10 studies[38]	**61** per 1000 **119** per 1000 Difference: **58 more per 1000** (95% CI, 5 more to 144 more)	**High**	Compared with placebo, filgrastim increases the risk of bone pain.

PICO (1.2)
Population: People with cancer treated with chemotherapy
Intervention: Pegfilgrastim
Comparator: Placebo

Outcome	Study results and measurements	Absolute effect estimates Placebo	 Pegfilgrastim	Quality of evidence	Summary
Febrile neutropenia	Odds ratio: 0.18 (95% CI, 0.06 to - 0.56) Based on data from 3251 participants in 7 studies[38]	**166** per 1000	**35** per 1000 Difference: **131 fewer per 1000** (95% CI, 154 fewer to 66 fewer)	**High**	Compared with placebo, pegfilgrastim reduces the risk of febrile neutropenia.
Bone pain	Odds ratio: 1.91 (95% CI, 1.27 to 2.87) Based on data from 3188 participants in 6 studies[38]	**124** per 1000	**213** per 1000 Difference: **89 more per 1000** (95% CI, 28 more to 165 more)	**High**	Compared with placebo, pegfilgrastim increases the risk of bone pain.

Clinical Question 2: Secondary Prophylaxis

PICO (2.1)

Population: Adults treated with systemic antineoplastic therapy for a solid tumor or lymphoma who experienced a neutropenic complication from a previous cycle of therapy (for which primary prophylaxis was not received)

Intervention: G-CSF

Comparator: Standard management (dose delay or dose reduction)

Outcome	Study results and measurements	Absolute effect estimates Standard management / G-CSF	Quality of evidence	Summary
Receipt of planned dose intensity	Odds ratio: 3.02 (95% CI, 1.98 to 4.61) Based on data from 407 participants in 1 study[15]	**500** per 1000 / **751** per 1000 Difference: **251 more per 1000** (95% CI, 164 more to 322 more)	**Moderate** Due to serious risk of bias[a]	Secondary prophylaxis with G-CSF probably improves receipt of planned dose intensity.
Adverse events	Based on data from 407 participants in 1 study[15]	Reported no significant differences in adverse events, but did not report specifically on grade 3 or higher	**Low** Due to very serious risk of bias[b]	Secondary prophylaxis with G-CSF may have little effect on adverse events.

a. **Risk of Bias: serious.** Trial stopped earlier than scheduled, resulting in potential for overestimating benefits.

b. **Risk of Bias: very serious.** Incomplete data in publication.

Clinical Question 3: Treatment of Febrile Neutropenia

PICO (3.1)

Population: Adults or children who develop febrile neutropenia during cancer treatment

Intervention: G-CSF or GM-CSF added to antibiotics

Comparator: Antibiotics alone

Outcome	**Study results and measurements**	**Absolute effect estimates**		**Quality of evidence**	**Summary**
		Antibiotics alone	G-CSF or GM-CSF added to antibiotics		
Overall mortality	Relative risk: 0.74 (95% CI, 0.47 to 1.16) Based on data from 1335 participants in 13 studies[50]	**70** per 1000	**52** per 1000 Difference: **18 fewer per 1000** (95% CI, 37 fewer to 11 more)	**High**	G-CSF or GM-CSF probably has little or no effect on overall mortality among patients with febrile neutropenia.
Hospitalized > 10 days	Relative risk: 0.65 (95% CI, 0.44 to 0.95) Based on data from 1087 participants in 7 studies[50]	**349** per 1000	**227** per 1000 Difference: **122 fewer per 1000** (95% CI, 195 fewer to 17 fewer)	**Moderate** Due to serious inconsistency	G-CSF or GM-CSF may reduce the likelihood of hospitalization for > 10 days.

Clinical Question 4: CSFs in the Setting of Progenitor Cell Transplantation

PICO (4.1)

Population: Multiple myeloma or lymphoma, stem cell mobilization

Intervention: G-CSF plus other agents

Comparator: G-CSF alone

Outcome	Study results	Quality of evidence	Summary
Yield of CD34+ cells	Compared with G-CSF alone, the following combinations are associated with higher yield of CD34+ cells: • G-CSF plus plerixafor[16] • G-CSF plus cyclophosphamide[18] • G-CSF plus intermediate-dose cytarabine[17] • G-CSF plus motixafortide[21]	**High** for plerixafor and chemotherapy. MODERATE for motixafortide due to fewer studies.	Compared with G-CSF alone, the combination of G-CSF with plerixafor, cyclophosphamide, intermediate-dose cytarabine, or motixafortide increases the yield of. CD34+ cells.

PICO (4.2)

Population: Patients Undergoing Autologous Stem Cell Transplantation

Intervention: G-CSF or GM-CSF after transplantation

Comparator: Placebo or usual care

Outcome	Study measurements	Results	Quality of evidence	Summary
Days to ANC $\geq$ 0.5 X 10^9/L	Lower better Based on data from participants in 17 studies[51]	Difference: **MD 4.08 lower** (95% CI, 5.03 lower to 3.13 lower)	**High**	G-CSF or GM-CSF shorten the time to neutrophil recovery after autologous stem cell transplantation.
Days to discharge	Lower better Based on data from participants in 15 studies[51]	Difference: **MD 2.92 lower** (95% CI, 3.86 lower to 1.99 lower)	**High**	G-CSF or GM-CSF shorten the time to discharge after autologous stem cell transplant.

PICO (4.3)

Population: Patients Undergoing Allogeneic Stem Cell Transplantation

Intervention: G-CSF or GM-CSF

Comparator: Placebo or usual care

Outcome	Study results and measurements	Results	Quality of evidence	Summary
Grade 2-4 GvHD	Based on data from participants in 6 studies[51]	Relative risk: 1.03 (95% CI, 0.81 to 1.31)	**Low** Due to very serious inconsistency[a]	G-CSF or GM-CSF may have little or no effect on the risk of grade 3 or 4 GVHD after allogeneic stem cell transplantation.
Days to ANC ≥ 0.5 X 10^9/L	Based on data from participants in 5 studies[51]	Mean difference: 3.53 lower (95% CI, 4.22 lower to 2.84 lower)	**High**	G-CSF or GM-CSF shorten the time to neutrophil recovery after allogeneic stem cell transplantation.
Days to discharge	Based on data from participants in 4 studies[51]	Mean difference: 2.02 lower (95% CI, 5.07 lower to 1.68 higher)	**Moderate** Due to serious imprecision	G-CSF or GM-CSF may have little or no effect on days to discharge after autologous stem cell transplant.

a. Inconsistency: very serious. RCTs and large observational studies have produced different results.

Clinical Question 5: CSFs with Concurrent Chemoradiotherapy

PICO (5.1)

Population: Patients receiving chemoradiotherapy for limited-stage SCLC

Intervention: GM-CSF

Comparator: Usual care

Outcome	Study results and measurements	Absolute effect estimates		Quality of evidence	Summary
		Usual care	GM-CSF		
Grade 3 or 4 thrombocytopenia	Based on data from 215 participants in 1 study[52]	**12** per 100	**54** per 100	**Low** Due to serious imprecision, Due to serious risk of bias[a]	GM-CSF may increase the risk of severe thrombocytopenia when administered with concurrent chemoradiotherapy.

a. Risk of Bias: serious. Some differences in study arm characteristics.; **Imprecision: serious.** Only data from one study.

PICO (5.2)

Population: Patients receiving chemoradiotherapy for nasopharyngeal cancer

Intervention: PEG-rhG-CSF

Comparator: No PEG-rhG-CSF

Outcome	Study results and measurements	Absolute effect estimates		Quality of evidence	Summary
		No PEG-rhG-CSF	PEG-rhG-CSF		
Grade 3 neutropenia	Based on data from 88 participants in 1 study[24]	**0** per 100	**13.6** per 100 *P* = 0.03	**Low** Due to serious risk of bias, Due to serious imprecision[a]	PEG-rhG-CSF during chemoradiotherapy may reduce the incidence of grade 3 neutropenia
Platelet levels	Based on data from 88 participants in 1 study[24]	Platelet levels did not differ significantly between study arms		**Very low** Due to serious risk of bias, Due to very serious imprecision[b]	PEG-rhG-CSF during concurrent chemoradiotherapy may not affect platelet levels, but there is uncertainty.

a. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: serious.** Only data from one study;

b. **Risk of Bias: serious.** Inadequate/lack of blinding of participants and personnel, resulting in potential for performance bias; **Imprecision: very serious.** Only data from one study, not the primary outcome of interest;

Clinical Question 6: Do G-CSFs differ with respect to safety or efficacy?

PICO (6.1)

Population: Adults with cancer

Intervention: G-CSF biosimilar

Comparator: Originator

Outcome	Study results and measurements	Absolute effect estimates Reference biologic vs G-CSF biosimilar	Quality of evidence	Summary
Neutropenia	Based on data from participants in 5 studies[27-31]	For outcomes such as febrile neutropenia, duration of severe neutropenia, and time to ANC recovery, RCTs and meta-analyses suggest that biosimilar CSFs are non-inferior to the reference biologic.	**High**	Biosimilar G-CSFs are probably non-inferior to the reference biologic with respect to efficacy.
Grade 3 or 4 adverse events	Based on data from participants in 6 studies[26-31]	Meta-analyses and RCTs suggested that differences in the frequency of grade 3 or 4 adverse events may be small, but statistical testing of the differences was often not performed.	**Moderate** Uncertainty due to lack of statistical testing in several publications	Biosimilars and reference biologics may have a similar frequency of grade 3 or grade 4 adverse events.

PICO (6.2) Pegylated G-CSF vs G-CSF

Population: Adults with cancer

Intervention: Pegylated G-CSF

Comparator: G-CSF

Outcome	Results	Quality of evidence	Summary
Febrile neutropenia	Three meta-analyses reported no significant difference in efficacy between pegylated G-CSF and G-CSF[36,37,39] and one reported higher efficacy with pegylated G-CSF than with G-CSF[38]	**Moderate** Due to serious inconsistency[a]	Pegylated G-CSF and G-CSF may have similar efficacy against febrile neutropenia.

Severe neutropenia	Two meta-analyses reported no significant difference in efficacy between pegylated G-CSF and G-CSF[37,38] (Li 2020; Wang 2019), and one reported higher efficacy with pegylated G-CSF than with G-CSF[36]	**Moderate** Due to serious inconsistency[a]	Pegylated G-CSF and G-CSF may have similar efficacy against severe neutropenia.
Bone pain	Two meta-analyses reported no significant difference in the incidence of bone pain between pegylated G-CSF and G-CSF[37,38] and one reported lower incidence with pegylated G-CSF than with G-CSF[36]	**Moderate** Due to serious inconsistency[a]	Pegylated G-CSF and G-CSF may be associated with a similar incidence of bone pain.

a. Inconsistency: serious. The direction of the effect is not consistent between the included studies

Clinical Question 7: Administration of CSFs

PICO (7.1)

Population: Non-Hodgkin's lymphoma, breast cancer, relapsed or refractory ovarian cancer, and advanced or metastatic non-small cell lung cancer.

Intervention: Same-day pegfilgrastim

Comparator: Day 2 pegfilgrastim

Outcome Timeframe	**Study results and measurements**	**Absolute effect estimates** Day 2 pegfilgrastim	Same-day pegfilgrastim	**Quality of evidence**	**Summary**
Area over the absolute neutrophil count time-response curve (AOC)	Based on data from 192 participants in 4 studies[53]	AOC was higher (worse) in same-day arm at AOC threshold of $<0.5 \times 10^9$/L. Difference was not statistically significant at AOC threshold of $<1.0 \times 10^9$/L.		**Low** Due to serious inconsistency, Due to serious imprecision[a]	Same-day pegfilgrastim may worsen severity and duration of absolute neutrophil count (ANC) suppression relative to next-day pegfilgrastim.

a. Inconsistency: serious. Results vary by AOC threshold; **Imprecision: serious.** Low number of patients.

Data Supplement 3: Search Strategy String and Dates

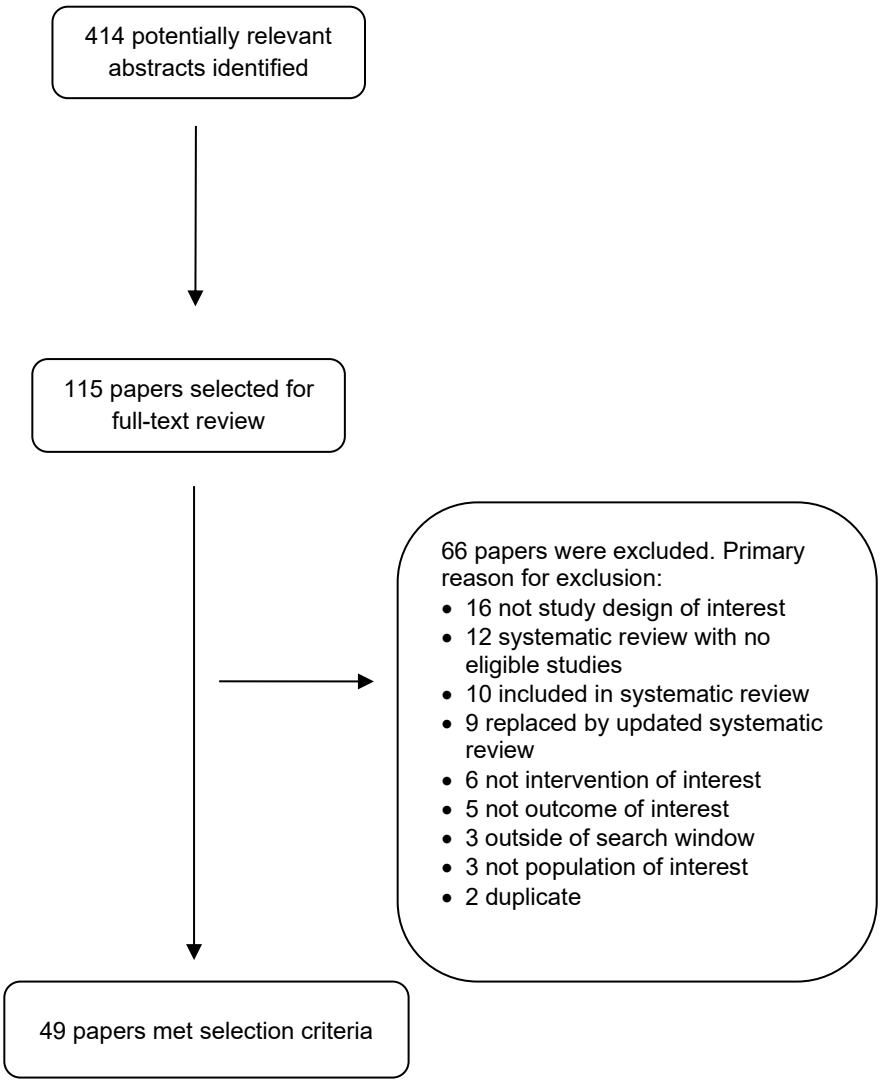
A computerized literature search of PubMed was performed. The search of the English-language literature published between September 1, 2014 and August 22, 2025 combined terms for colony stimulating factors in combination with terms for cancer and hematopoietic stem cell transplantation. Results of the databases searches were supplemented with hand searching of the bibliographies of systematic reviews and selected seminal articles.

Search strategy:

(Colony-stimulating factors OR G-CSF OR GM-CSF OR filgrastim OR pegfilgrastim OR sargramostim OR eflapegrastim OR efbemalenograstim) AND (Neoplasms OR Hematopoietic Stem Cell Transplantation)

Filters: Randomized controlled trial, systematic review, meta-analysis, guideline; English language

Data Supplement 4: QUOROM Diagram



Data Supplement 5: GLIDES Action Verb Glossary

Prescribe	***Prepare***	***Test***	***Monitor***	***Conclude***	***Perform***	***Educate/ Counsel***
add	address	assess	arrange	assess	confine	adhere
adjust	adhere	begin	ascertain	base	ensure	advise
administer	adjust	carry out	assess	conclude	follow	benefit
advance	adopt	check	check	consider	give	clarify
apply	analyze	conduct	conduct	contact	implement	counsel
attempt	attempt	continue	continue	coordinate	include	deliver
avoid	be (aware)	determine	determine	determine	incorporate	discuss
change	become	do	evaluate	diagnose	indicate	educate
choose	begin	evaluate	examine	distinguish	inspect	enable
continue	collect	have	follow up	exclude	offer	encourage
desensitize	continue	identify	have	give (attention)	operate	explain
dilute	dedicate	indicate	include	recognize	perform	have
discontinue	define	measure	institute	recommend	place	help
exercise	develop	need	maintain	respect	receive	identify
improve	encourage	obtain	manage	review	recommend	include
increase	engage	offer	monitor	suspect	relate	incorporate
indicate	ensure	perform	obtain	take (into account)	resect	inform
individualize	establish	prefer	occur	use	reserve	instruct
influence	form	receive	offer	weigh	select	involve
initiate	have	recommend	perform		start	modify
institute	identify	repeat	provide		treat	negotiate
manage	include	require	reassess		undergo	offer
offer	incorporate	reserve	receive		use	promote
order	initiate	restore	recommend			protect
prefer	institute	screen	repeat			provide
prescribe	know	take	require			receive
provide	lead	test	review			recommend
receive	perform	trigger	screen			reinforce
recommend	plan	undergo	warrant			review
reduce	prepare	use				start
repeat	recommend	utilize				support
replace	review					teach
reserve	share					tell
restart	train					use
review	understand					
start	undertake					
suggest	use					
supplement						
taper						
titrate						
treat						
use						
utilize						
warrant						

Dispose	***Document***	***Advocate***	***Examine***	***Inquire***	***Prevent***	***Refer/Consult***
admit	complete	advocate	assess	ask	administer	assess
dispose	document	encourage	auscultate	assess	avoid	conduct
hospitalize	identify	endorse	examine	complete	cleanse	consult
guide	notate	ensure	include	conduct	combine	manage
observe		focus	inspect	gather	continue	obtain
refer		recommend	palpate	include	discard	offer
		work (to)	percuss	incorporate	encourage	recommend
			perform	inquire	give	refer
			use	obtain	immunize	seek
				review	minimize	work
				screen	practice	(together)
				verify	prevent	
					provide	
					receive	
					recommend	
					use	

Glossary from the GuideLines Into Decision Support (GLIDES) project, https://medicine.yale.edu/cmi/glides/.

General Note. ASCO Guideline recommendations (strong or conditional/weak) and terminology represent reasonable options for patients depending on clinical circumstances and in the context of individual patient preferences. Recommended care should be accessible to patients whenever possible.

Data Supplement 6: Abbreviations

- AE, adverse event
- ANC, absolute neutrophil count
- AOC, area over the absolute neutrophil count time-response curve
- ASCT, autologous stem cell transplant
- BID, twice a day
- CI, confidence interval
- CrI, credibility interval from Bayesian meta-analysis
- CSF, colony-stimulating factors
- CY, cyclophosphamide
- DSN, duration of severe neutropenia
- EFS, event-free survival
- FEC-D, fluorouracil, epirubicin, cyclophosphamide, docetaxel
- FOLFIRI, leucovorin, 5-fluorouracil, irinotecan
- FOLFOX, leucovorin, 5-fluorouracil, oxaliplatin
- FN, febrile neutropenia
- G-CSF, granulocyte colony-stimulating factors
- GM-CSF, granulocyte macrophage colony-stimulating factors
- GvHD, graft-versus-host disease
- HR, hazard ratio
- HSCT, hematopoietic stem cell transplant
- ID-AraC, intermediate-dose cytarabine
- ITT, intention-to-treat
- LOS, length of stay
- MD, mean difference
- MM, multiple myeloma
- NE, neutropenic event
- NHL, non-Hodgkin lymphoma
- NR, not reported
- NS, non-significant
- NSCLC, non-small-cell lung cancer
- OR, odds ratio
- OS, overall survival
- P, pertuzumab
- PEG-rhG-CSF, pegylated recombinant human granulocyte colony-stimulating factor
- PFS, progression-free survival
- PICO, population, intervention, comparator, outcome
- PP-CSF, primary prophylactic colony-stimulating factor
- QD, once a day
- RCHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone
- RCT, randomized controlled trial
- RD, reduced dose
- RDI, relative dose intensity
- rhG-CSF, recombinant human granulocyte colony-stimulating factor
- RR, relative risk
- RT, radiation therapy
- SCLC, small-cell lung cancer
- SD, standard dose
- SMD, standardized mean difference
- SOE, standard order entry
- TA, docetaxel and doxorubicin
- TAC, docetaxel, doxorubicin, and cyclophosphamide
- TC, docetaxel and cyclophosphamide
- TCH, docetaxel, carboplatin, and trastuzumab
- TEAEs, treatment-emergent adverse events
- VRd, bortezomib, lenalidomide, and dexamethasone
- WBC, white blood cell
- WMD, weighted mean difference
- YF-H-2015005, new CXCR4 antagonist

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