

Appendix 3 (as supplied by the authors): Detailed description of included clinical trials

Author, year, country	Eligibility: previous ESA therapy, Hb (g/dL)	Type of tumour (%), stage (%)	Surgery, previous chemo (%), chemo/radio on study	Design: sample size, treatment (wk) [follow-up (mo)], Hb target (g/dL), control [iron co-intervention]	ESA regimen: type, initial dose, schedule, route	Demographics: mean age (y), male (%), mean Hb (g/dL)
Aapro ⁵³ 2008 Asia, Central/South America, Europe	No <12.9	Solid (breast) -	No 47 Non-platinum	463 24[18 mo] Increase ≥ 2 g/L compared to baseline None [PRN]	Beta 30,000 U QW SC	57 0 11.3
Gordon ⁶⁴ 2008 USA	No ≤11	Both (non-myeloid malignancy) I-II (25), III-IV (58), Limited (2), Extensive (1), Unknown (14)	No 32 None	218 12 11 None [PRN]	Darbe 6.75 µg/kg Q4W SC	70 36 10.1
Smith ⁶⁵ 2008 Europe, North America, Australia	No ≤11	Solid (NSCLC, breast, prostate, colon, kidney, ovarian, cervix, stomach, head and neck, pancreas, SCLC, bladder, soft tissue sarcoma, other) (86) Hematological (MM, NHL, other) (14) Solid: I (2), II (8), III (22), IV (60), NR (8); Hematological: MM: I (7), II (16), III (54), Unknown (24); NHL: Indolent (69), Aggressive (31)	No 70 None	989 [2 y] ≥ 12 Placebo [-]	Darbe 6.75 µg/kg Q4W SC	64 51 9.5
Strauss ⁵⁴ 2008 Germany	No 9-13	Solid (cervical) IB (1), IIB (54), IIIB (38), IVA (5), IVB (1) [‡]	No - Platinum & radiotherapy	74 12 ≥14 None [PRN]	Beta 150 U/kg TIW SC	49 0 11.5
Thomas ⁵⁵ 2008 Canada, USA, The Netherlands	- <14	Solid (cervical) IIB (70), IIIB (26), IVA (5)	No - Platinum & radiotherapy	109 [37 mo] ≥12 None [-]	Alpha 40,000 U QW SC	48 0 -
Anon ⁶⁰ 2007 Western Europe, Australia, North America	No 9-13	Solid (SCLC) Extensive	No - Platinum & etoposide	549 24 ≥14 Placebo [-]	Darbe 300 µg QW -	61 65 11.9
Charu ⁶¹ 2007 USA	No ≤11	Solid (breast, lung, other) (73) Hematological (lymphoid) (27) I/II (19), III/IV (62), NR (19)	No 100 ^{†††} None	287 12 - None [no]	Darbe 3.0 µg/kg Q2W SC	71 41 10.1

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Kotasek ^{62*} 2007 Australia, Canada, New Zealand, Western Europe	No ≤11	Solid (breast, lung, other) (68) Hematological (32) 32 I/II (11), III/IV (79), NR (11)	No - Cytotoxic	727 16 [max 30 d] 11-13 Placebo [-]	Darbe 2.25; 4.5 µg/kg QW SC	61 41 9.6
Machtay ⁵¹ 2007 USA, Canada	- 9-13.5 M, 9-12.5 W	Solid (squamous cell carcinoma of the head and neck) I (18), II (18), III (18), IV (47) [§]	No 30 Radiotherapy ^{***}	148 During radiotherapy [min 2 y] - None [yes]	Alpha 40,000 U QW SC	63 74 12.1
Overgaard ⁶³ 2007 Denmark	- <14	Solid (head, neck) -	No - Radiotherapy	515 - >15.5 None [-]	Darbe 150 µg QW SC	- - -
Wright ⁵² 2007 Canada	No ≤12	Solid (NSCLC) IIIA/IIIB T3 or 4 (61), N2 or 3 (50), M1 (51) ^{**}	No 23 Platinum & radiotherapy	70 12 [max 60 wk] 12-14 Placebo [yes]	Alpha 40,000 U QW SC	69 53 10.3
Anon A ⁴⁹ 2006 China	- 9-11	Hematological (MM, low-grade NHL, CLL) -	No 100 Yes	60 12 - None [yes]	Beta 150 U/kg TIW SC	- - -
Anon B ⁴⁸ 2006 China	- Participants described as anemic	Solid -	No 100 Platinum	121 12 - None [yes]	Beta 150 U/kg TIW SC	- - -
Wilkinson ⁵⁰ 2006 Western Europe	- ≤12	Solid (ovarian) I (13), II (9), III (52), IV (24), NR (2)	No - Platinum (75), platinum & paclitaxel (25)	182 Max 28 - None [PRN]	Alpha 10,000 U TIW SC	60 0 10.7
Chang ⁴³ 2005 Canada	- ≤12	Solid (breast) I (14), II (61), III (17), IV (7), NR (1)	No - Myelotoxic	354 Max 28 [max 2 y] 12 None [yes]	Alpha 40,000 U QW SC	50 0 11.3
Christodoulakis ^{44*} 2005 Greece	- 9-12	Solid (colorectal) A&B (44), C&D (45), NR (11) ^{††}	Yes - None	223 25 d perioperative - None [yes]	Alpha 150; 300 U/kg SID SC	71 44 10.6
Mystakidou ⁴⁵ 2005 Greece	- ≤11	Solid (pancreatic, genital system, lung, colon) -	No 0 None	100 24 [max 6] - None [yes]	Alpha 40,000 U QW SC	64 39 10.0

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O'Shaughnessy ⁴⁶ 2005 USA	No 9-14	Solid (breast) I (28), IIA (36), IIB (14), IIIA (8), IIB (8)	No - Non-platinum	100 12 [6] - Placebo [yes]	Alpha 40,000 U QW SC	54 0 12.9
Savonije ³ The Netherlands	- ≤12.1	Solid (NSCLC, SCLC, upper GI tract, gynecologic, other) -	No - Platinum	316 Max 4 (after 2-6 chemo cycles) [max 12] - None [yes]	Alpha 10,000 U TIW SC	57 56 10.7
Taylor ⁵⁹ 2005 Australia, New Zealand, USA	- <11	Solid (breast, colon, NSCLC, other) (89) Hematological (NHL, other) 11 -	- 100 Yes	386 - 11-13 Placebo [-]	Darbe 300 µg Q3W -	- - 10.0
Witzig ⁴⁷ 2005 USA	No <11.5 M, <10.5 F	Solid (lung, breast, other) -	No - Platinum (17) & non-platinum (83)	344 16 [1 y] - Placebo [yes]	Alpha 40,000 U QW SC	64 44 9.6
Bamias ³⁶ 2003 Greece	- ≤13	Solid (ovarian, NSCLC, SCLC, other) -	No 24 Platinum	144 12 - None [-]	Alpha 10,000 U TIW SC	61 51 11.5
Boogaerts ³⁷ 2003 Western Europe, South Africa	- ≤11	Solid (ovarian, bone, skin, breast, digestive organs, respiratory, other) (44) Hematological (MM, NHL, CLL) (56) -	No 74 Yes	262 12 - None [yes]	Beta 150 U/kg TIW SC	62 37 9.1
Hedenus ⁵⁷ 2003 Europe, Australia, Canada	No ≤11	Hematological (Hodgkin's disease, NHL, CLL, MM) -	No 100 Yes	349 12 [-11] - Placebo [PRN]	Darbe 2.25 µg/kg QW SC	65 48 9.5
Henke ³⁸ 2003 Western Europe	- <13 M, <12 F	Solid (head & neck) I (2), II (2), III (24), IV (74)	No - Radiotherapy	351 10-14 d pre and during radiotherapy [6 wk post radiotherapy] 15 M, 14 F Placebo [yes]	Beta 300 U/kg TIW SC	58 87 11.7
Iconomou ³⁹ 2003 Greece	- ≤11	Solid (lung, breast, colorectal, ovarian, unknown primary, kidney, stomach, other) -	No - Platinum (42) & non-platinum (58)	122 12 - None [yes]	Alpha 10,000 U TIW SC	62 42 10.1

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Janinis ⁴⁰ 2003 Greece	- ≤11	Solid -	No - Platinum & non-platinum	372 - - None [yes]	Alpha 10,000 U TIW -	- - 10.5
Kosmadakis ⁴¹ 2003 Greece	- 8.5-13	Solid (gastrointestinal) -	Yes - None	75 2 perioperatively [1 y] - Placebo [yes]	Alpha 300 U/kg SID SC	67 54 10.9
Kotasek ^{58*} 2003 Australia, Canada, Costa Rica, Europe	No ≤11	Solid (breast, gynecologic, gastrointestinal, lung, other) -	No - Yes	249 12 - Placebo [-]	Darbe 4.0; 6.75; 9.0; 12.0; 13.5; 15.0 µg/kg Q3W SC	58 29 9.9
Recasens ⁴² 2003 Spain	- <12 M, <11 F	Hematological (MM) -	No - -	91 8 - None [-]	Alpha 10,000 U TIW SC	68 45 -
Huddart ³² 2002 United Kingdom	- <10.5	Solid -	No - Platinum	90 3-6 chemo cycles + 4 wk - None [-]	Alpha 10,000 U TIW SC	- - -
Osterborg ³³ 2002 Russia, Western Europe	- <10	Hematological (Low grade NHL, MM or CLL) -	No - Yes	349 16 - Placebo [yes]	Beta 150 U/kg TIW SC	64 50 9.3
Pronzato ³⁴ 2002 Western Europe	- 10-12	Solid (breast) IV (47)	No 100 Yes	178 Max 28 - None [-]	Alpha 10,000 – 20,000 U TIW -	54 0 10.8
Thomas ³⁵ 2002 United Kingdom	- ≤12	- -	No - Yes	130 Max 28 - None [-]	Alpha 10,000 U TIW -	- - 10.6
Vansteenkiste ⁵⁶ 2002 Australia, Canada, Europe	No ≤11	Solid (SCLC, NSCLC) SCLC: limited (11), extensive (18) NSCLC: I (1), II (1), III (25), IV (44)	No - Platinum	320 12 [mean 1 y] - Placebo [-]	Darbe 2.25 µg/kg QW SC	61 71 10.1
Dammacco ³⁰ 2001 Western Europe, Israel	- <11	Hematological (MM) IA (5), IB (1), IIA (34), IIB (2), IIIA (50), IIIB (9) ^{††}	No 99 Non-platinum	145 12 - Placebo [-]	Alpha 150 U/kg TIW SC	66 45 9.5
Littlewood ³¹ 2001 Europe, South Africa	- ≤10.5	Solid (breast, gastrointestinal, other) (54) Hematological (NHL, Myeloma, CLL) (46) -	No 92 Non-platinum	375 Max 28 [median 26] - Placebo [yes]	Alpha 150 U/kg TIW SC	59 33 9.8

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Qvist ²⁹ 1999 Denmark	No ≤13.7	Solid (colorectal) -	Yes - None	100 1 perioperatively [4 wk post discharge] - None [yes]	Alpha 150 U/kg SID SC	69 40 12.2
Anon ²³ 1998 -	- <12 [†]	Solid (breast, ovarian, SCLC, esophagus, prostate) (64) Hematological (MM, lymphoma) (36) -	No Some Platinum (27) & non-platinum (73)	201 12 ≥12 Placebo [-]	Alpha 150 U/kg TIW SC	- - -
Dammacco ²⁴ 1998 Italy	- <10	Hematological (MM) II (27), IIIA (72), NR (1)	No 100 Non-platinum	71 24 - None [PRN]	Alpha 150 U/kg TIW SC	65 49 7.9
Ferrini ²⁵ 1998 Italy	- <9	Hematological (low risk MDS) -	No - None	87 8 - Placebo [yes]	Alpha 150 U/kg SID -	65 57 -
Kettelhack ²⁶ 1998 Germany	- 8.5-13.5	Solid (colonic) -	Yes - None	109 1-2 perioperatively [3] - Placebo [PRN]	Beta 20,000 U SID SC	69 42 11.8
Oberhoff ²⁷ 1998 Europe	- ≤11	Solid (gynecologic, breast, lung, urinary tract cancer, gastrointestinal, other)	No 61 Platinum (>50) & non-platinum	227 12 - None [-]	Beta 5,000 U SID SC	54 26 9.9
ten Bokkel Huinink ^{28*} 1998 The Netherlands, Germany	No <13	Solid (ovarian carcinoma) II (11), III (73), IV (16)	No 99 Platinum	122 Max 24 [11] - None [-]	Beta 150; 300 U/kg TIW SC	60 - 12.0
Osterborg ^{21*} 1996 Europe	- <10	Hematological (MM, CLL, low-grade NHL) MM: I (2), II (12), III (39), unknown (1) CLL: III (6), IV (15), unknown (1) NHL: I (1), III (2), IV (21), NR (1)	No 88 Non-platinum	144 24 11-13 None [-]	Beta 2,000; 10,000 U SID SC	65 57 8.0
Park ²² 1996 Korea	- Participants described as "anemic"	Solid (lung, gastrointestinal) -	No - Yes	90 12 - None [-]	Alpha 150 U/kg TIW SC	- - -

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Cazzola ^{20*} 1995 Europe	- ≤11	Hematological (NHL, MM) MM: III (52) ^{‡‡} NHL: IV (55) ^{§§}	No - 80	146 8 - None [PRN]	Beta 1,000; 2,000; 5,000; 10,000 U SID SC	68 49 9.4
Cascinu ¹⁸ 1994 Italy	- <9	Solid (stomach, ovary, melanoma, head and neck, lung, breast) -	No 0 Platinum	100 9 10 Placebo [PRN]	Alpha 100 U/kg TIW SC	58 53 8.7
Rose ¹⁹ 1994 USA	- <10.5	Hematological (CLL) III/IV ^{***}	No - PRN	221 Max 12 12-13.5 Placebo [-]	Alpha 150 U/kg TIW SC	- - 9.4
Abels ¹⁷ 1993 A USA	- ≤10.5	No myeloid malignancy or acute leukemia Advanced	No 0 None	124 Max 8 - Placebo [-]	Alpha 100 U/kg TIW SC	- - -
Abels ¹⁷ 1993 B USA	- ≤10.5	Solid (breast, gynecologic, gastrointestinal, lung, prostate, head and neck) (59) Hematologic (41) -	No 100 Non-platinum	157 Max 12 - Placebo [-]	Alpha 150 U/kg TIW SC	64 41 -
Abels ¹⁷ 1993 C USA	- ≤10.5	No myeloid malignancy or acute leukemia Advanced	No 100 Platinum	132 Max 12 - Placebo [-]	Alpha 150 U/kg TIW SC	- - -

Note: ESA = erythropoietic-stimulating agent; USA = United States of America; Anon = anonymous; Hb = hemoglobin; "-" indicates that the value was not reported in the study; M = men; W = women; NSCLC = non-small cell lung cancer; SCLC = small cell lung cancer; MM = multiple myeloma; NHL = non-Hodgkin's lymphoma; NR = study listed as "not reported"; CLL = chronic lymphocytic leukemia; GI = gastrointestinal; MDS = myelodysplastic syndrome; PRN = as necessary; QW = once per week; SC = subcutaneous; Q4W = every 4 weeks; TIW = thrice per week; Q2W = every 2 weeks; SID = once per day; Q3W = every 3 weeks.

*Study also includes dose comparison.

†Or decrease of ≥ 1.5 g/dL since beginning of chemo course.

‡FIGO (Federation of Gynecology and Obstetrics) staging.

§American Joint Committee on Cancer Staging.

**TNM (Tumour, Node, Metastasis) staging.

††Dukes' staging.

‡‡Durie & Salmon staging.

§§Ann Arbor staging.

***Rai Staging.

†††May include radiotherapy.

‡‡‡Concurrent chemoradiotherapy options allowed.