

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Landgren O, Thomas A, Mailankody S. Myeloma and second primary cancers. *N Engl J Med* 2011;365:2241-2.

**TABLE-1. Selected studies focusing on second malignancies following multiple myeloma**

Study	Study design (study period)	Pts, n	% with second malignancy	Multiple myeloma to second malignancy, median time	Hematologic malignancy, n	Solid tumor, n
<sup>a</sup> Mailankody et al., 2011	Population-based registry study (1986-2005)	8740	1.4%	45.3 months (AML/MDS)	69	508
<sup>b</sup> Hasskarl et al, 2011	Retrospective study, single institution (1997-2008)	589	3%	35 months	6	12
<sup>c</sup> Attal, et al., 2010*	Randomized phase III trial, maintenance lenalidomide vs. placebo after high-dose melphalan/ASCT	614	5.5% (lenalidomide maintenance) 1% (placebo)	44 months	# Lenalidomide maintenance: 11 # Placebo arm: 3	# Lenalidomide maintenance: 12 # Placebo arm: 3
<sup>d</sup> McCarthy et al., 2010*	Randomized phase III trial, maintenance lenalidomide vs. placebo after high-dose melphalan/ASCT	460	6.5% (lenalidomide maintenance) 2.6% (placebo)	17.5 months after ASCT	# Lenalidomide maintenance: 8 # Placebo arm: 0	# Lenalidomide maintenance: 10 # Placebo arm: 4
<sup>e</sup> Palumbo et al., 2010*	Randomized phase III trial, maintenance lenalidomide vs. placebo after low-dose melphalan/prednisone+/-lenalidomide	459	3.9% (lenalidomide maintenance) 1.3% (placebo)	25 months	# MPR-R arm: 7 # MPR arm: 5 # MP arm: 1	# MPR-R: 5 # MPR: 4 # MP: 3
<sup>f</sup> Barlogie et al, 2008	Retrospective study, single institution (1989-2007)	2418	1%	NR	26	NR
<sup>g</sup> Finnish Leukemia Group, 2000	Retrospective study based on patients from clinical trials (1979-1985)	432	9.2%	37 months (solid tumors) 56 months (acute leukemia)	17	23
<sup>h</sup> Govindarajan et al, 1996	Prospective study (NR)	188	3.7%	63 months	7	NR
<sup>i</sup> Cuzick et al, 1987	Retrospective study based on patients from clinical trials (1964-1975)	648	1.8%	82 months	12	NR
<sup>j</sup> Bergsagel et al, 1979	Prospective study (1973-1977)	364	3.8%	NR	14	NR
<sup>k</sup> Kyle et al., 1970	Case series (1965-1966)	3	N/A	45 months	3	NR
<sup>l</sup> Edwards and Zawadski, 1966	Case series (1950-1966)	8	N/A	10 years	1	NR
<sup>m</sup> Nordenson, 1966	Retrospective study, multi institution (1932-1963)	310	2.2%	NR	7	NR

**Legend:** \* These results come from interim analyses presented at the American Society of Hematology meeting in Orlando, Florida, December 2010. # Updated numbers from presentations at the International Myeloma Workshop in Paris, France, May 2011. At this time, the final analyses and written reports have not yet been published.

References: <sup>a</sup>Mailankody S, Pfeiffer RM, Kristinsson SY, et al. Risk of acute myeloid leukemia and myelodysplastic syndromes following multiple myeloma and its precursor disease (MGUS). *Blood* 2011;118:4086-92. <sup>b</sup>Hasskarl J, Ihorst G, De Pasquale D, et al. Association of multiple myeloma with different neoplasms: systematic analysis in consecutive patients with myeloma. *Leuk Lymphoma* 2011;52:247-59. <sup>c</sup>Attal M, Lauwers VC, Marit G, et al. Maintenance Treatment with Lenalidomide After Transplantation for Myeloma: Final Analysis of the IFM 2005-02. *Blood* 2010;116:310. <sup>d</sup>McCarthy PL, Owzar K, Anderson KC, et al. Phase III Intergroup Study of Lenalidomide Versus Placebo Maintenance Therapy Following Single Autologous Hematopoietic Stem Cell Transplantation (AHSCT) for Multiple Myeloma: CALGB 100104. *Blood* 2010;116:37. <sup>e</sup>Palumbo A, Bringhen S, Cavalli M, et al. A Phase 3 Study Evaluating the Efficacy and Safety of Lenalidomide Combined with Melphalan and Prednisone In Patients 65 Years with Newly Diagnosed Multiple Myeloma (NDMM): Continuous Use of Lenalidomide Vs Fixed-Duration Regimens. *Blood* 2010;116:622. <sup>f</sup>Barlogie B, Tricot G, Haessler J, et al. Cytogenetically defined myelodysplasia after melphalan-based autotransplantation for multiple myeloma linked to poor hematopoietic stem-cell mobilization: the Arkansas experience in more than 3,000 patients treated since 1989. *Blood* 2008;111:94-100. <sup>g</sup>Acute leukaemia and other secondary neoplasms in patients treated with conventional chemotherapy for multiple myeloma: a Finnish Leukaemia Group study. *European journal of haematology* 2000;65:123-7. <sup>h</sup>Govindarajan R, Jagannath S, Flick JT, et al. Preceding standard therapy is the likely cause of MDS after autotransplants for multiple myeloma. *British journal of haematology* 1996;95:349-53. <sup>i</sup>Cuzick J, Erskine S, Edelman D, Galton DA. A comparison of the incidence of the myelodysplastic syndrome and acute myeloid leukaemia following melphalan and cyclophosphamide treatment for myelomatosis. A report to the Medical Research Council's working party on leukaemia in adults. *British journal of cancer*

1987;55:523-9. <sup>j</sup>Bergsagel DE, Bailey AJ, Langley GR, MacDonald RN, White DF, Miller AB. The chemotherapy on plasma-cell myeloma and the incidence of acute leukemia. The New England journal of medicine 1979;301:743-8. <sup>k</sup>Kyle RA, Pierre RV, Bayrd ED. Multiple myeloma and acute myelomonocytic leukemia. The New England journal of medicine 1970;283:1121-5. <sup>l</sup>Edwards GA, Zawadzki ZA. Extrasosseous lesions in plasma cell myeloma. A report of six cases. Am J Med. 1967 Aug;43(2):194-205. <sup>m</sup>Nordenson NG. Myelomatosis. A clinical review of 310 cases. Acta Medica Scandinavica Supplementum 1966;445:178-86.

**Abbreviations:** MDS = myelodysplastic syndrome; AML = acute myeloid leukemia; ASCT = autologous stem cell transplantation; NR = not reported; MPR-R = melphalan/ prednisone, revlimid (lenalidomide), with revlimid maintenance; MPR = melphalan/ prednisone, revlimid (lenalidomide), without revlimid maintenance; MP = melphalan/ prednisone, without revlimid maintenance.