

Supplementary Online Content

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

eTable 1. Characteristics of Included Studies

First Author	FDA Notification Year	Indication	Therapy	Therapy Type	Primary Endpoint	HR OS	HR PFS	Median OS Difference (months)	Median PFS Difference (months)
Amadori	2016	Acute Myeloid Leukemia	Gemtuzumab	T	OS	0.69	NR	1.30	NR
Attal	2012	Myeloma	Lenalidomide	T	PFS	1.25	0.50	NR	18.00
Bang	2010	Gastric Cancer	Trastuzumab	T + C	OS	0.74	0.71	2.70	1.20
Baselga	2012	Advanced Breast Cancer	Everolimus	T	PFS	NR	0.36	NR	6.50
Baselga	2012	Advanced Breast Cancer	Pertuzumab	T	PFS	0.64	0.62	NR	6.10
Bellmunt	2017	Advanced Urothelial Cancer	Pembrolizumab	I	OS/PFS	0.71	0.98	2.90	-1.20
Bennouna	2013	Metastatic Colorectal Cancer	Bevacizumab	T	OS	0.81	0.67	1.40	1.6
Borghaei	2015	Non-Small Cell Lung Cancer	Nivolumab	I	OS	0.73	0.92	2.8	1.9
Brahmer	2015	Non-Small Cell Lung Cancer	Nivolumab	I	OS	0.59	0.62	3.2	0.7
Brose	2014	Metastatic Thyroid Cancer	Sorafenib	T	PFS	0.80	0.59	NR	5.00
Bruix	2017	Hepatocellular Carcinoma	Regorafenib	T	OS	0.63	0.46	2.80	1.60
Burger	2011	Advanced Ovarian Cancer	Bevacizumab	T	PFS	0.92	0.72	0.40	3.80
Caplin	2014	Entero-pancreatic Endocrine Tumours	Lanreotide	T	PFS	NR	0.47	NR	9.00
Cappuzzo	2010	Non-Small Cell Lung Cancer	Erlotinib	T	PFS	0.81	0.69	1.00	0.29
Chapman	2012	Metastatic Melanoma	Vemurafenib	T	OS/PFS	0.37	0.26	2.20	3.70
Chouieri	2015	Metastatic Renal Cell Carcinoma	Cabozantinib	T	PFS	0.67	0.58	-2.80	3.60
Cicenas	2016	Non-Small Cell Lung Cancer	Erlotinib	T	OS	1.02	0.94	0.20	0.23
Ciuleanu	2009	Non-Small Cell Lung Cancer	Pemetrexed	C	PFS	0.79	0.60	2.80	2.00
Cortes	2011	Metastatic Breast Cancer	Eribulin mesylate	C	OS	0.81	0.87	2.50	1.50
Cristofanill	2016	Metastatic Breast Cancer	Palbociclib	T	PFS	NR	0.46	NR	4.90
De Bono	2010	Metastatic Castration Resistant Prostate Cancer	Cabazitaxel	C	OS	0.70	0.74	2.40	1.40
Demetri	2013	Gastrointestinal Stromal Tumors	Regorafenib	T	PFS	0.77	0.27	NA	3.90
Demetri	2016	Leiomyosarcoma	Trabectedin	C	OS	0.87	0.55	0.50	2.70
Dimopoulos	2007	Multiple Myeloma	Lenalidomide	T	TTP	0.66	0.35	14.50	6.60
Dimopoulos	2016	Multiple Myeloma	Daratumumab	I	PFS	NR	0.37	NR	2.50
Eisenberger	2017	Metastatic Castration Resistant Prostate Cancer	Cabazitaxel	C	OS	1.02	1.10	NR	NR
Elisei	2013	Medullary Thyroid Cancer	Cabozantinib	T	PFS	NR	0.28	NA	7.20
Ferris	2016	Metastatic Head and Neck Carcinoma	Nivolumab	I	OS	0.70	0.89	2.40	0.30
Finn	2016	Metastatic Breast Cancer	Palbociclib	T	PFS	NR	0.58	NR	10.30

Fizazi	2012	Metastatic Castration Resistant Prostate Cancer	Abiraterone	H	OS	0.74	0.66	4.60	1.90
Flaherty	2012	Metastatic Melanoma	Trametinib	T	PFS	0.54	0.45	NR	3.30
Fuchs	2013	Advanced Gastric Cancer	Ramucirumab	T	OS	0.78	0.48	1.40	0.80
Furman	2014	Chronic Lymphocytic Leukemia	Idelalisib	T	PFS	0.28	0.15	NA	8.5
Garon	2014	Non-Small Cell Lung Cancer	Ramucirumab	T	OS	0.86	0.76	1.40	1.50
Goede	2014	Chronic Lymphocytic Leukemia	Obinutuzumab	T	PFS	0.41	0.18	NA	15.60
Grothey	2013	Metastatic Colorectal Cancer	Regorafenib	T	OS	0.77	0.49	1.40	0.20
Hallek	2010	Chronic B-Cell Lymphocytic Leukemia	Rituximab	T	PFS	0.67	0.48	NR	19.10
Hauschild	2012	Metastatic Melanoma	Dabrafenib	T	PFS	0.61	0.30	NR	2.40
Herbst	2016	Non-Small Cell Lung Cancer	Pembrolizumab	T	PFS	0.61	0.79	1.90	0.10
Hillmen	2013	Chronic Lymphocytic Leukemia	Ofatumumab	T	PFS	0.91	0.57	NR	9.30
Hodi	2010	Metastatic Melanoma	Ipilimumab	I	OS	0.68	0.81	3.60	0.00
Hortobagyi	2012	Advanced Breast Cancer	Ribociclib	T	PFS	NR	0.56	NR	7.30
Hudes	2007	Metastatic Renal Cell Carcinoma	Temsozilumab	T	OS	0.73	NR	1.10	1.60
Johnston	2010	Metastatic Breast Cancer	Lapatinib	T	PFS	NR	0.86	NR	1.10
Jonker	2007	Metastatic Colorectal Cancer	Cetuximab	T	OS	0.77	0.68	1.50	0.10
Kantarjian	2016	Acute Lymphoblastic Leukemia	Inotuzumab	T	OS	0.77	0.45	0.60	3.20
Kantarjian	2017	Acute Lymphoblastic Leukemia	Blinatumomab	T	OS	0.71	NR	3.70	NR
Larkin	2014	Metastatic Melanoma	Cobimetinib	T	OS/PFS	0.65	0.51	NA	3.7
Llovet	2008	Hepatocellular Carcinoma	Sorafenib	T	OS/PFS	0.69	1.08	2.8	-0.2
Long	2015	Melanoma	Trametinib	T	PFS	0.71	0.67	6.4	2.2
Lonial	2015	Multiple Myeloma	Elotuzumab	T	PFS	NR	0.70	NA	4.5
Marcus	2017	Non-Hodgkin's Lymphoma	Obinutuzumab	T	PFS	0.75	0.66	NR	NR
Mayer	2015	Metastatic Colorectal Cancer	TAS-102	C	OS	0.68	0.48	1.80	0.30
Miller	2007	Metastatic Breast Cancer	Bevacizumab	T	PFS	0.88	0.60	1.50	5.90
Mirza	2016	Ovarian Cancer	Niraparib	T	PFS	NR	0.27	NR	5.60
Mok	2016	Non-Small Cell Lung Cancer	Osimertinib	T	PFS	NR	0.30	NR	5.70
Moreau	2016	Multiple Myeloma	Ixazomib	T	PFS	NR	0.74	NR	5.90
Moskowitz	2015	Hodgkin's Lymphoma	Brentuximab Vedotin	T	PFS	1.15	0.57	NR	18.80
Motzer	2009	Metastatic Renal Cell Carcinoma	Sunitinib	T	PFS	0.65	0.42	NR	6.00
Motzer	2010	Metastatic Renal Cell Carcinoma	Everolimus	T	PFS	0.87	0.32	0.40	3.03
Motzer	2015	Metastatic Renal Cell Carcinoma	Nivolumab	I	OS	0.73	0.88	5.40	0.20
Orlowski	2007	Multiple Myeloma	Doxorubicin	C	TTP	0.71	0.59	NR	2.80
Palumbo	2016	Multiple Myeloma	Daratumumab	T	PFS	NR	0.39	NR	7.80
Paz-Ares	2013	Non-Small Cell Lung Cancer	Pemetrexed	C	PFS	0.78	0.60	2.90	1.30
Peters	2017	Non-Small Cell Lung Cancer	Alectinib	T	PFS	0.76	0.47	NR	15.30
Pfisterer	2006	Ovarian cancer	Gemcitabine	C	PFS	0.96	0.72	0.70	2.8

Posner	2007	Head and Neck Cancer	Docetaxel	C	OS	0.70	0.71	41.00	23.00
Pujade-Lauraine	2014	Ovarian Cancer	Avastin	T	PFS	0.85	0.48	3.30	3.30
Pujade-Lauraine	2017	Ovarian Cancer	Olaparib	T	PFS	NR	0.30	NR	13.60
Raymond	2011	Pancreatic Islet Cell Tumors	Sunitinib	T	PFS	0.41	0.42	NR	5.90
Reck	2016	Non-Small Cell Lung Cancer	Nintedanib	T	PFS	0.94	0.79	1.00	1.30
Rini	2011	Metastatic Renal Cell Carcinoma	Axitinib	T	PFS	NR	0.67	NR	2.00
Rittmeyer	2016	Non-Small Cell Lung Cancer	Atezolizumab	I	OS	0.73	0.95	4.20	-1.20
Robert	2015	Advanced Melanoma	Dabrafenib	T	OS	0.69	0.56	3.80	4.10
Robert	2015	Advanced Melanoma	Pembrolizumab	I	OS/PFS	0.69	0.58	NR	1.30
Rosell	2012	Non-Small Cell Lung Cancer	Tarceva	T	PFS	1.04	0.37	-0.20	4.20
Ryan	2013	Metastatic Castration Resistant Prostate Cancer	Abiraterone	H	OS/PFS	0.81	0.53	4.4	8.20
Salles	2012	Follicular Lymphoma	Rituximab	T	PFS	0.87	0.55	NR	5.70
San Miguel	2008	Multiple Myeloma	Bortezomib	T	PFS	0.70	NR	13.3	NR
San-Miguel	2014	Multiple Myeloma	Panobinostat	T	PFS	0.87	0.63	3.25	3.91
Scher	2012	Metastatic Castration Resistant Prostate Cancer	Enzalutamide	H	OS	0.63	0.40	13.60	2.90
Schlumberger	2015	Thyroid Cancer	Lenvatinib	T	PFS	0.62	0.21	NR	14.70
Schoffski	2016	Soft Tissue Sarcoma	Eribulin	C	OS	0.77	0.88	2.00	0.00
Sehn	2016	Non-Hodgkin's Lymphoma	Obinutuzumab	T	PFS	0.82	0.52	NR	33.10
Sequist	2013	Non-Small Cell Lung Cancer	Afatinib	T	PFS	NR	0.58	NR	4.64
Shaw	2013	Non-Small Cell Lung Cancer	Crizotinib	T	PFS	1.02	0.49	-2.50	4.70
Sledge	2017	Advanced Breast Cancer	Abemaciclib	T	PFS	NR	0.55	NR	10.20
Soria	2017	Non-small Cell Lung Cancer	Ceritinib	T	PFS	0.73	0.55	7.80	8.50
Sternberg	2010	Metastatic Renal Cell Carcinoma	Pazopanib	T	PFS	NR	0.46	NR	5.00
Stewart	2014	Multiple Myeloma	Carfilzomib	T	PFS	0.79	0.69	0.00	8.70
Stone	2017	Acute Myeloid Leukemia	Midostaurin	T	OS	0.78	NR	49.10	NR
Tabernero	2015	Metastatic Colorectal Cancer	Ramucirumab	T	OS	0.84	0.79	1.60	1.20
Tewari	2014	Advanced Cervical Cancer	Bevacizumab	T	OS	0.68	NR	3.20	NR
Thatcher	2015	Non-Small Cell Lung Cancer	Necitumumab	T	OS	0.84	0.85	1.60	0.20
Van Cutsem	2007	Metastatic Colorectal Cancer	Panitumumab	T	PFS	1.00	0.54	0.22	0.18
Van Cutsem	2012	Metastatic Colorectal Cancer	Aflibercept	T	OS	0.82	0.76	0.90	2.23
Van der Graaf	2012	Soft Tissue Sarcoma	Pazopanib	T	PFS	0.86	0.31	1.80	3.00
Van Oers	2015	Chronic Lymphocytic Leukemia	Ofatumumab	T	PFS	0.85	0.50	NR	14.20
Verma	2012	Metastatic Breast Cancer	Trastuzumab	T + C	OS/PFS	0.68	0.65	5.80	3.20
Vermorken	2007	Head and Neck Cancer	Docetaxel	C	PFS	0.73	0.72	4.30	2.80
Vermorken	2008	Head and Neck Cancer	Cetuximab	T	OS	0.80	0.54	2.70	2.30

Von Hoff	2013	Metastatic Pancreatic Cancer	Paclitaxel	C	OS	0.72	0.69	1.80	1.80
Wang-Gillam	2016	Metastatic Pancreatic Cancer	Irinotecan	C	OS	0.67	0.56	1.90	1.60
Weber	2015	Advanced Melanoma	Nivolumab	I	OS/PFS	NR	0.82	NR	0.43
Wells	2012	Metastatic Medullary Thyroid Cancer	Vandetanib	T	PFS	0.89	0.46	NR	10.70
Wilke	2014	Gastric Adenocarcinoma	Ramucirumab	T	OS	0.81	0.64	2.20	1.50
Yao	2016	Neuroendocrine Tumors	Everolimus	T	PFS	0.64	0.48	NR	8.50

T, Targeted Agent; C, Chemotherapy; I, Immunotherapy; H, Hormone therapy; OS, Overall survival; PFS, Progression-free survival; TTP, Time to progression; NR, Not Reported.

eTable 2. Framework Scores and RMST Difference Values

Study	ASCO-CBS					ESMO-PMCBG					RMST Difference (in months)	
	OS	PFS	Framework Endpoint	Framework	Framework + TOC	OS	PFS	Framework Endpoint	Framework	Framework + TOC	OS	PFS
Amadori 2016	31.0	NA	OS	31.0	51.0	Not Scored – Hematology RCT					2.48	NA
Attal 2012	-25.0	40.0	OS	-25.0	-25.0	Not Scored – Hematology RCT					NA	6.52
Bang 2010	26.0	23.2	OS	26.0	26.0	3	2	OS	3	3	2.70	2.07
Baselga 2012	NA	51.2	PFS	51.2	67.2	NA	3	PFS	3	4	NA	3.30
Baselga 2012	36.0	30.4	OS	36.0	52.0	NA	3	PFS	3	4	2.50	4.30
Bellmunt 2017	29.0	1.6	OS	29.0	47.0	3	1	OS	3	3	1.66	0.63
Bennouna 2013	19.0	26.4	OS	19.0	19.0	1	3	OS	1	1	1.98	1.66
Borghaei 2015	27.0	6.4	OS	27.0	27.0	4	1	OS	4	4	1.82	1.20
Brahmer 2015	41.0	30.4	OS	41.0	61.0	4	2	OS	4	4	3.57	2.28
Brose 2014	20.0	32.8	PFS	32.8	32.8	NA	3	PFS	3	4	1.33	3.76
Burger 2011	8.5	22.6	PFS	22.6	22.6	1	1	PFS	1	1	1.38	2.00
Bruix 2017	37.0	43.2	OS	37.0	57.0	4	3	OS	4	4	3.32	2.58
Caplin 2014	NA	42.4	PFS	42.4	42.4	NA	3	PFS	3	4	-0.81	3.15
Cappuzzo 2010	19.0	24.8	PFS	24.8	24.8	1	2	PFS	2	2	1.99	1.47
Chapman 2012	63.0	59.2	PFS	59.2	75.2	3	3	OS	3	3	1.30	2.67
Chouieri 2015	33.0	33.6	OS	33.0	49.0	1	3	PFS	3	3	1.09	2.25
Cicenas 2016	-2.0	4.8	OS	-2.0	-2.0	NA	NA	NA	NA	NA	-0.24	0.27
Ciuleanu 2009	21.0	32.0	PFS	32.0	48.0	3	3	PFS	3	3	2.52	1.90
Cristofanilli 2016	NA	43.2	PFS	43.2	59.2	NA	3	PFS	3	4	NA	2.62
Cortes 2011	19.0	10.4	OS	19.0	19.0	2	1	OS	2	2	0.86	0.55
De Bono 2010	30.0	20.8	OS	30.0	30.0	2	2	OS	2	2	2.41	1.05

Demetri 2013	23.0	58.4	PFS	58.4	74.4	NA	3	PFS	3	3	0.32	2.01
Dimopoulos 2007	34.0	52.0	OS	34.0	34.0	Not Scored – Hematology RCT					2.84	NA
Dimopoulos 2016	NA	50.4	PFS	50.4	50.4	Not Scored – Hematology RCT					2.82	3.28
Demetri 2016	13.0	36.0	OS	13.0	29.0	1	3	OS	NA	NA	0.24	2.02
Eisenberger 2017	-2.4	-7.9	OS	-2.4	-2.4	NA	NA	NA	NA	NA	-0.37	-0.38
Elisei 2013	NA	57.6	PFS	57.6	57.6	NA	3	PFS	3	4	NA	5.09
Ferris 2016	30.0	8.8	OS	30.0	50.0	3	1	OS	3	3	1.69	0.42
Finn 2016	NA	33.6	PFS	33.6	49.6	NA	3	PFS	3	4	NA	4.67
Fizazi 2012	26.0	27.2	OS	26.0	26.0	4	2	OS	4	4	1.97	NA
Flaherty 2012	46.0	44.0	PFS	44.0	60.0	NA	3	PFS	3	3	0.69	2.09
Fuchs 2013	22.4	41.4	OS	22.4	42.4	1	2	OS	1	1	1.56	1.58
Furman 2014	72.0	68.0	OS	72.0	72.0	Not Scored – Hematology RCT					1.44	5.60
Garon 2014	14.0	19.2	OS	14.0	14.0	1	1	OS	1	1	1.48	1.20
Goede 2014	59.0	65.6	PFS	65.6	65.6	Not Scored – Hematology RCT					2.86	11.14
Grothey 2013	23.0	40.8	OS	23.0	23.0	1	2	OS	1	1	-0.08	1.21
Hallek 2010	33.0	41.6	OS	33.0	33.0	Not Scored – Hematology RCT					3.28	8.57
Hauschild 2012	39.0	56.0	PFS	56.0	72.0	NA	3	PFS	3	3	NA	2.09
Herbst 2016	29.0	9.6	OS	29.0	49.0	2	1	OS	2	2	1.74	0.70
Hillmen 2013	9.0	34.4	PFS	34.4	50.4	Not Scored – Hematology RCT					1.40	6.02
Hortobagyi 2012	NA	35.2	PFS	35.2	35.2	NA	3	PFS	3	3	NA	2.71
Hodi 2010	32.0	15.2	OS	32.0	52.0	4	1	OS	4	4	4.61	1.33
Hudes 2007	27.0	NA	OS	27.0	43.0	1	NA	OS	1	1	0.73	1.42
Johnston 2010	NA	11.2	PFS	11.2	11.2	NA	1	PFS	1	1	2.92	NA
Jonker 2007	23.0	25.6	PFS	25.6	25.6	2	2	OS	2	2	1.33	0.47
Kantarjian 2016	23.0	44.0	OS	23.0	39.0	Not Scored – Hematology RCT					3.79	3.10
Kantarjian 2017	29.0	NA	OS	29.0	49.0	Not Scored – Hematology RCT					1.72	NA
Larkin 2014	36.0	39.2	OS	36.0	52.0	NA	3	PFS	3	3	0.89	1.94

Llovet 2008	31.0	-6.4	OS	31.0	31.0	3	1	OS	3	3	1.44	NA
Long 2015	29.0	26.4	OS	29.0	45.0	4	2	PFS	2	2	2.33	3.30
Lonial 2015	NA	24.0	PFS	24.0	40.0	Not Scored – Hematology RCT					NA	3.39
Marcus 2017	25.0	27.2	OS	25.0	25.0	Not Scored – Hematology RCT					0.75	3.09
Mayer 2015	32.0	41.6	OS	32.0	52.0	2	2	OS	2	2	1.79	1.45
Miller 2007	12.0	32.0	OS	12.0	28.0	1	3	PFS	3	4	1.91	4.82
Mirza 2016	NA	58.4	PFS	58.4	89.0	NA	3	PFS	3	4	NA	3.25
Mok 2016	NA	56.0	PFS	56.0	56.0	NA	3	PFS	3	4	NA	3.65
Moreau 2016	NA	20.8	PFS	20.8	26.0	Not Scored – Hematology RCT					NA	1.44
Moskowitz 2015	-15.0	34.4	OS	-15.0	-15.0	Not Scored – Hematology RCT					-0.71	8.81
Motzer 2009	35.0	46.4	PFS	46.4	62.4	NA	3	PFS	3	3	2.45	2.66
Motzer 2010	13.0	54.4	PFS	54.4	54.4	1	3	PFS	3	3	0.36	2.52
Motzer 2015	27.0	9.6	OS	27.0	27.0	4	1	OS	4	4	2.28	1.04
Orlowski 2007	29.0	33.0	OS	29.0	29.0	Not Scored – Hematology RCT					1.29	1.76
Palumbo 2016	NA	48.8	PFS	48.8	48.8	Not Scored – Hematology RCT					NA	2.52
Paz-Ares 2013	22.0	32.0	PFS	32.0	32.0	4	2	PFS	2	2	2.44	2.86
Pfisterer 2006	4.0	22.4	OS	4.0	4.0	1	3	PFS	3	3	0.59	2.16
Posner 2007	30.0	23.2	OS	30.0	30.0	4	3	OS	4	4	7.54	8.21
Peters 2017	24.0	42.4	OS	24.0	40.0	NA	3	PFS	3	4	0.74	3.33
Pujade-Lauraine 2014	15.0	41.6	PFS	41.6	57.6	3	3	PFS	3	4	1.70	3.19
Pujade-Lauraine 2017	NA	56.0	PFS	56.0	72.0	NA	3	PFS	3	4	NA	7.28
Raymond 2011	59.0	46.4	OS	59.0	59.0	NA	3	PFS	3	4	3.13	5.62
Reck 2016	6.0	16.8	PFS	16.8	16.8	1	1	PFS	1	1	1.85	3.62
Rittmeyer 2016	27.0	4.0	OS	27.0	47.0	4	1	OS	4	4	2.35	NA
Rini 2011	NA	26.8	PFS	26.8	49.5	NA	3	PFS	3	4	NA	2.08
Robert 2015	31.0	35.2	OS	31.0	47.0	3	3	OS	3	3	1.48	2.41
Robert 2015	31.0	33.6	OS	31.0	47.0	NA	3	PFS	3	3	1.57	1.74

Ryan 2013	19.0	37.6	PFS	37.6	37.6	2	3	OS	2	2	2.05	5.03
Rosell 2012	-4.0	50.4	PFS	50.4	50.4	1	3	PFS	3	4	NA	5.25
Salles 2012	13.0	36.0	OS	13.0	13.0	Not Scored – Hematology RCT					NA	6.14
San Miguel 2008	39.0	41.6	OS	39.0	39.0	Not Scored – Hematology RCT					2.20	4.23
San-Miguel 2014	13.0	29.6	OS	13.0	13.0	Not Scored – Hematology RCT					1.14	3.75
Schlumberger 2015	38.0	63.2	PFS	63.2	79.2	NA	3	PFS	NA	NA	NA	10.40
Scher 2012	37.0	48.0	OS	37.0	53.0	3	3	OS	3	3	2.66	4.44
Sehn 2016	18.0	38.4	OS	18.0	34.0	Not Scored – Hematology RCT					2.22	6.96
Sequist 2013	NA	33.6	PFS	33.6	49.6	NA	3	PFS	3	3	NA	4.22
Shaw 2013	-2.0	40.8	PFS	40.8	56.8	1	3	PFS	3	4	NA	3.52
Soria 2017	27.0	36.0	PFS	36.0	52.0	3	3	PFS	3	4	2.26	5.48
Stewart 2014	21.0	24.8	OS	21.0	21.0	Not Scored – Hematology RCT					2.26	4.25
Stone 2017	22.0	NA	OS	22.0	22.0	Not Scored – Hematology RCT					5.90	NA
Sternberg 2010	NA	43.2	PFS	43.2	59.2	NA	3	PFS	3	4	NA	3.80
Sledge 2017	NA	35.8	PFS	35.8	51.8	NA	3	PFS	3	4	NA	4.28
Schoffski 2016	23.0	9.6	OS	23.0	23.0	3	2	OS	3	3	1.85	0.65
Taberero 2015	15.6	16.6	OS	15.6	15.6	1	1	OS	NA	NA	1.58	1.19
Tewari 2014	32.0	NA	OS	32.0	NA	3	NA	OS	3	3	2.25	NA
Thatcher 2015	16.0	12.0	OS	16.0	16.0	1	1	OS	1	1	1.44	0.63
Van Cutsem 2007	0.0	36.8	PFS	36.8	36.8	1	2	PFS	2	3	0.08	3.21
Van Cutsem 2012	18.3	19.4	OS	18.3	18.3	1	1	OS	1	1	2.03	NA
Van der Graaf 2012	14.0	55.2	OS	14.0	14.0	2	3	PFS	3	3	1.19	2.78
Van Oers 2015	15.0	40.0	OS	15.0	15.0	Not Scored – Hematology RCT					-0.27	5.82
Verma 2012	32.0	28.0	OS	32.0	48.0	2	3	OS	2	2	2.56	3.29
Vermorken 2007	27.0	22.4	OS	27.0	27.0	4	2	PFS	2	2	4.50	3.37
Vermorken 2008	20.0	36.8	OS	20.0	20.0	3	3	OS	3	3	1.66	1.91
Von Hoff 2013	28.0	24.8	OS	28.0	44.0	2	3	OS	2	2	1.83	1.27

Wang-gillam 2016	33.0	35.2	OS	33.0	53.0	2	3	OS	2	2	1.50	1.75
Weber 2015	NA	14.4	PFS	14.4	14.4	NA	2	PFS	2	2	NA	0.76
Wells 2012	11.0	43.2	OS	11.0	11.0	NA	3	PFS	3	4	0.79	4.89
Yao 2016	36.0	41.6	OS	36.0	52.0	NA	3	PFS	3	4	2.04	3.91
Wilke 2014	19.3	29.2	OS	19.3	19.3	2	3	OS	2	2	1.34	1.86

ASCO-CBS, ASCO Clinical Benefit Score; ESMO-PMCBG, ESMO Preliminary Magnitude of Clinical Benefit Grade; RMST, Restricted Mean Survival Time; OS, Overall survival; PFS, Progression-free survival; TOC, Tail of Curve Bonus (ASCO) or Long-term plateau (ESMO); NA, Not Applicable – these values were either not reported or could not be calculated. Framework endpoints represent the endpoints that were used to score the study using each framework (not necessarily the primary endpoint of the study). When calculating ASCO scores, if the reported HR in the trial was greater than 1, the ASCO score would be negative. Despite this negative score, these trials were used for drug approvals since the endpoints used for scoring in this analysis may not correspond to the endpoint used by the FDA in the approval process.

eTable 3. Mean RMST Differences (Months) for ESMO-PMCBGs Ranging From 1 to 4

ESMO-PMCBG	OS	PFS	Framework	Framework + TOC
1	1.19	1.21	1.64	1.47
2	1.69	1.84	2.02	2.21
3	1.94	3.51	3.13	2.18
4	3.34	NA	3.43	3.96

ESMO-PMCBGs, ESMO Preliminary Magnitude of Clinical Benefit Grades; OS, Overall Survival; PFS, Progression free survival; TOC, Tail-of-curve bonus (ASCO) or long term plateau (ESMO); NA, Not Applicable – No studies had a ESMO-PMCBG (PFS only) of 4. Endpoints used to calculate ESMO-PMCBGs are presented in the first row.

eTable 4. ICC Values

Endpoint	ICC (95 % CI)
ASCO OS	0.94 (0.91 – 0.96)
ASCO PFS	0.98 (0.97 – 0.99)
ASCO FR	0.82 (0.74 – 0.87)
ASCO FR + TOC	0.82 (0.74 – 0.87)
ESMO OS	0.96 (0.94 – 0.98)
ESMO PFS	0.90 (0.84 – 0.93)
ESMO FR	0.84 (0.76 – 0.90)
ESMO FR + TOC	0.72 (0.60 – 0.82)
RMST difference OS	0.96 (0.95 – 0.98)
RMST difference PFS	0.94 (0.91 – 0.96)

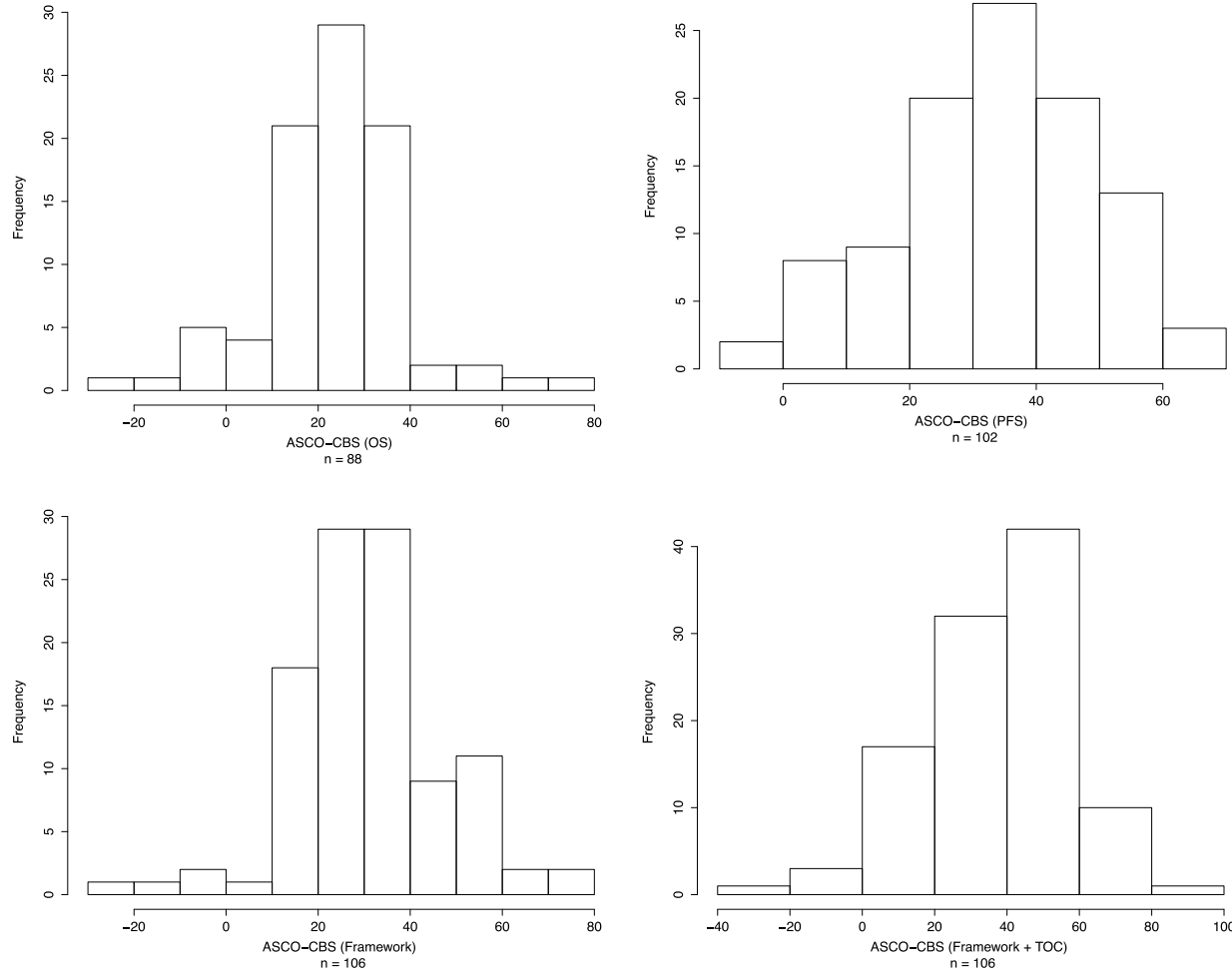
ICC, Intraclass Correlation Coefficient; OS, Overall Survival; PFS, Progression-free Survival; FR, Framework defined endpoint; FR + TOC, Framework defined endpoint + Tail of curve bonus; RMST, Restricted Mean Survival Time.

eTable 5. Primary Analysis With OS and PFS Data Split

OS Comparison	Spearman Correlation (95% CI)
ASCO-CBS vs HR	-1
ASCO-CBS + TOC vs HR	-0.90 (-0.96, -0.81)
ASCO-CBS vs mOS	0.44 (0.10, 0.64)
ASCO-CBS + TOC vs mOS	0.23 (-0.02, 0.49)
ASCO-CBS vs RMST	0.52 (0.28, 0.70)
ASCO-CBS + TOC vs RMST	0.44 (0.20, 0.64)
ESMO-PMCBG vs HR	-0.32 (-0.56, -0.02)
ESMO-PMCBG + TOC vs HR	-0.32 (-0.58, -0.02)
ESMO-PMCBG vs mOS	0.71 (0.35, 0.88)
ESMO-PMCBG + TOC vs mOS	0.71 (0.37, 0.87)
ESMO-PMCBG vs RMST	0.56 (0.33, 0.73)
ESMO-PMCBG + TOC vs RMST	0.56 (0.27, 0.73)
PFS Comparison	Spearman Correlation (95% CI)
ASCO-CBS vs HR	-1
ASCO-CBS + TOC vs HR	-0.88 (-0.94, -0.79)
ASCO-CBS vs mPFS	0.42 (0.08, 0.67)
ASCO-CBS + TOC vs mPFS	0.42 (0.09, 0.67)
ASCO-CBS vs RMST	0.34 (-0.02, 0.63)
ASCO-CBS + TOC vs RMST	0.33 (-0.03, 0.62)
ESMO-PMCBG vs HR	-0.55 (-0.73, -0.31)
ESMO-PMCBG + TOC vs HR	-0.37 (-0.61, 0.06)
ESMO-PMCBG vs mPFS	0.55 (0.36, 0.72)
ESMO-PMCBG + TOC vs mPFS	0.71 (0.49, 0.83)
ESMO-PMCBG vs RMST	0.33 (0.02, 0.58)
ESMO-PMCBG + TOC vs RMST	0.70 (0.45, 0.84)

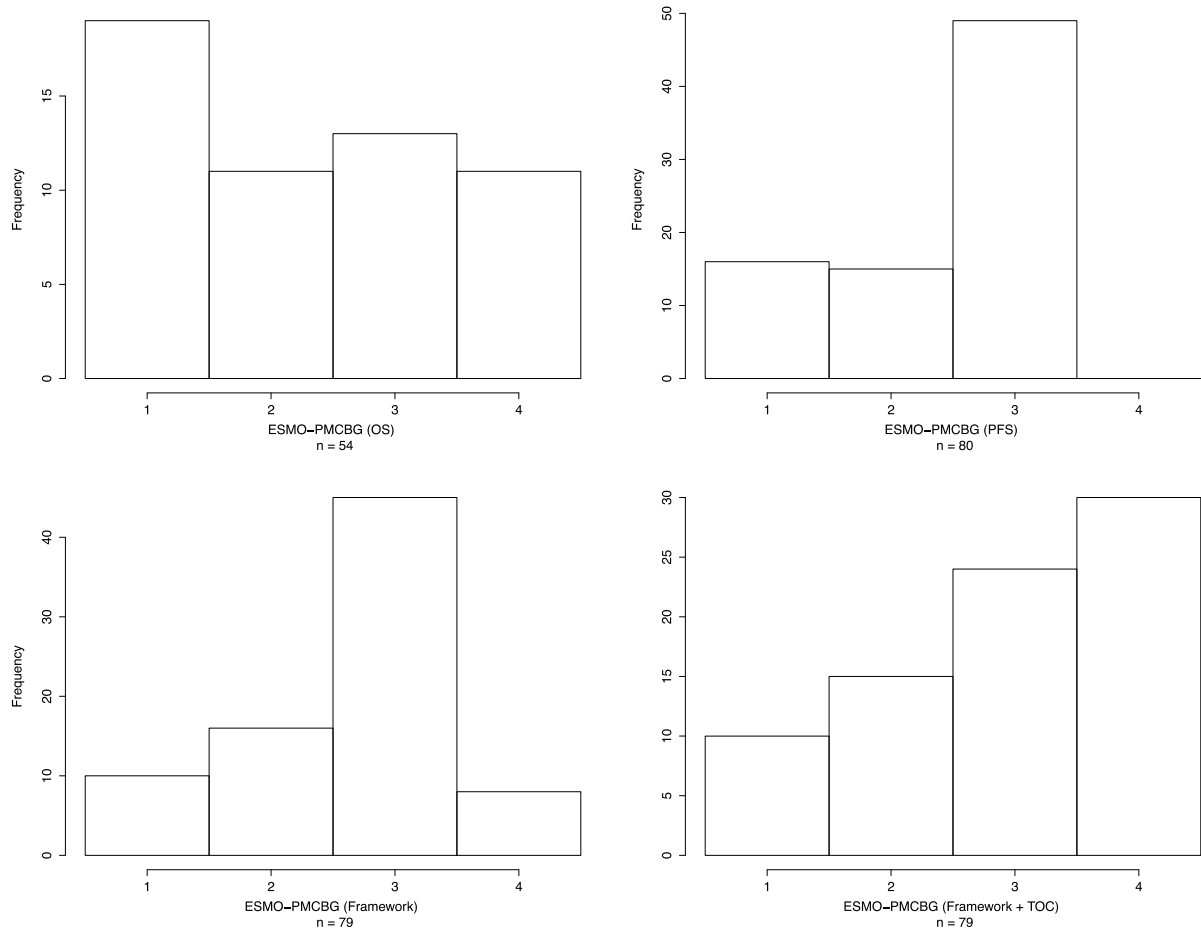
ASCO-CBS, ASCO Clinical Benefit Score; HR, Hazard Ratio; TOC, Tail-of-curve bonus; RMST, Restricted Mean Survival Time; mOS, median overall survival difference; mPFS, median progression-free survival difference; OS, overall survival; PFS, progression-free survival.

eFigure 1. Distribution of ASCO-CBS



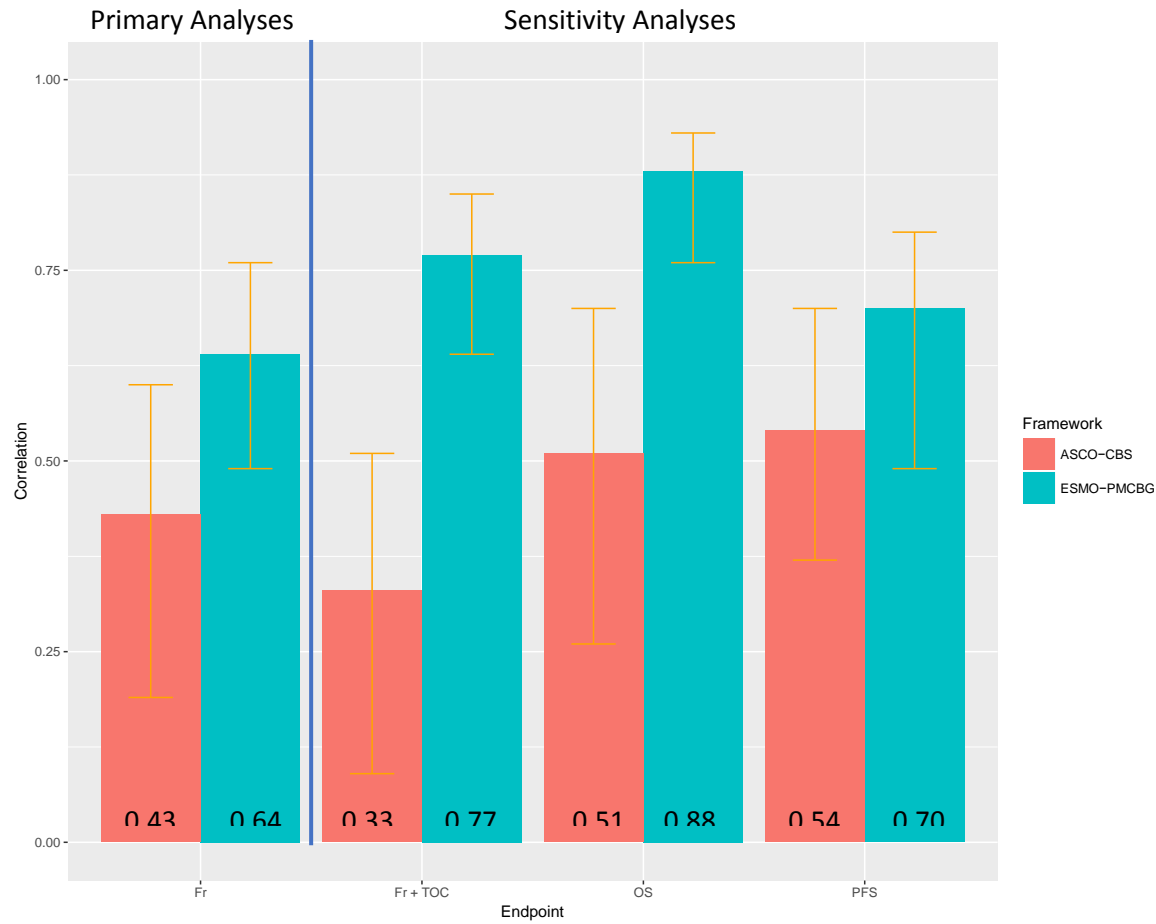
ASCO-CBS, ASCO Clinical Benefit Score; OS, Overall Survival; PFS, Progression-free Survival; TOC, Tail of Curve bonus. The number of scored studies using each endpoint are listed below each histogram (n). Framework represents studies scored using the ASCO framework criteria.

eFigure 2. Distribution of ESMO-PMCBG



ESMO-PMCBG, ESMO Preliminary Magnitude of Clinical Benefit Grade; OS, Overall Survival; PFS, Progression-free Survival; TOC, Tail of Curve bonus. The number of scored studies using each endpoint are listed below each histogram (n). Framework represents studies scored using the ESMO framework criteria.

eFigure 3. Spearman Correlations of ASCO Clinical Benefit Score (ASCO-CBS) and ESMO Preliminary Magnitude of Clinical Benefit Grade (ESMO-PMCBG) vs Median Survival Difference



Spearman correlations of ASCO Clinical Benefit Score (ASCO-CBS) and ESMO Preliminary Magnitude of Clinical Benefit Grade (ESMO-PMCBG) versus median survival difference. The values shown in each bar represent the point estimate of the spearman correlation. 95% confidence intervals are also illustrated on the graph. Fr, Framework defined endpoint; Fr + TOC, Framework defined endpoint including Tail-of-Curve bonus; OS, Overall Survival; PFS, Progression-free Survival.