

Supplementary material for Petrelli F, et al. Prognostic role of lactate dehydrogenase in solid tumors: A systematic review and meta-analysis of 76 studies. *Acta Oncol* 2015;54:961–70.

Supplementary Table I. Characteristics of included studies.

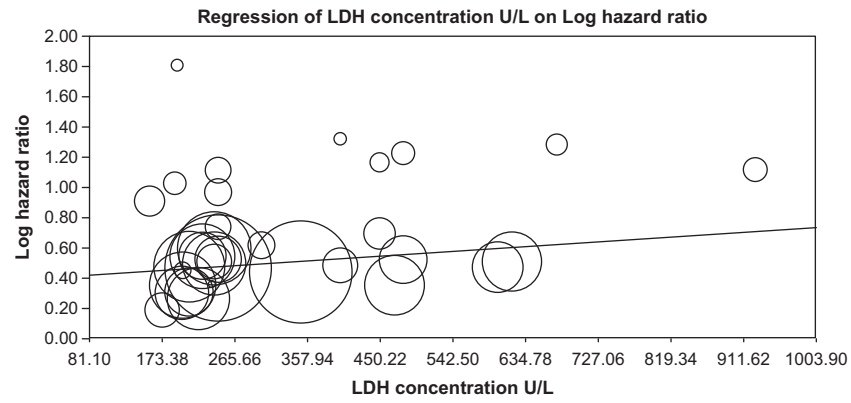
Author/year	Type of study	No. pts	Disease site	Disease stage	Cut-off for LDH	OS HR (p.)	PFS HR (p.)	DFS HR
Chibaudel/2011	Prospective	803	Colon	Metastatic	$>1 \times \text{ULN}$	1.8 (0.001)	–	–
Sougioultzis/2011	Retrospective	310	Gastric	Metastatic	225	1.72 (0.000)	–	–
Zhao/2014	Retrospective	365	Gastric	I-IV	157	2.476 (0.001)	–	2.209 (0.004)
Furuse/2009	Retrospective	85	Biliopancreatic	IV	300	1.85 (0.043)	–	–
Haas/2013	Retrospective	247	Pancreatic	Advanced or metastatic	250	1.21 (0.321)	1.13 (0.678)	–
Masaki/2005	Prospective	35	Pancreatic	Advanced or metastatic	NR	1.010 (0.001)	1.007 (0.007)	–
Nakay/2010	Prospective	108	Pancreatic	Advanced or metastatic	per 100 U/l increase	1.29 (0.030)	–	–
Yamaguchi/2014	Retrospective	258	NEC of the digestive system	Advanced or metastatic	$>1 \times \text{ULN}$	0.65 (0.021)	–	–
Jin/2013	Retrospective	689	NPC	Metastatic	245	1.595 ( $<0.001$ )	–	–
Li/2012	Prospective	533	NPC	I-IV	240	1.66 (0.033)	–	–
Tian/2013	Retrospective	85	NPC	Metastatic	245	2.09 (0.01)	–	–
Wan/2013	Prospective	400	NPC	Locally advanced	245	2.627 (0.002)	–	2.285 (0.001)
Wei/2014	Retrospective	601	NPC	I-IV	225	1.724 (0.002)	–	1.482 (0.014)
Zeng/2012	Retrospective	234	NPC	Metastatic	245	1.686 (0.004)	–	–
Zhou/2011	Retrospective	465	NPC	I-IV	245	3.038 ( $<0.001$ )	–	2.435 (0.004)
Almasi/2012	Prospective	85	SCLC	LD/ED	450	2 (0.004)	–	–
Ando/2014	Retrospective	57	SCLC	LD/ED	200	1.567 (0.35)	–	–
de Jong/2007	Retrospective	156	SCLC	LD/ED	$>1 \times \text{ULN}$	1.35 (0.002)	–	–
Kang/2014	Retrospective	187	SCLC	LD/ED	$>1 \times \text{ULN}$	1.507 (0.016)	1.658 (0.002)	–
Lee/2014	Retrospective	40	SCLC	LD	400	3.74 (0.037)	–	2.78 (0.043)
Najmi/2014	Retrospective	60	MPM	Advanced or metastatic	NR	1.01 (0.014)	–	–
Ulas/2014	Retrospective	462	NSCLC	IIIB/IV	$>1 \times \text{ULN}$	1.31 (0.047)	–	–
Wang/2014	Retrospective	114	SCLC	LD/ED	240	1.811 (0.001)	–	–
Wu/2014	Retrospective	90	Thymic carcinoma	III/IV	190	2.787 (0.004)	4.633 (0.000)	–
Liu/2014	Prospective	2425	Breast	I-III	469	1.42 (0.001)	–	–
Chiaron-Sileni/2004	Prospective	140	Melanoma	Advanced	$>1 \times \text{ULN}$	3.20 (0.0001)	–	–
Franzke/1998	Prospective	97	Melanoma	Metastatic	240	0.61 (0.002)	–	–
Gaudy-Marqueste/2014	Retrospective	126	Melanoma	Metastatic	$>1 \times \text{ULN}$	0.866 (0.674)	–	–
Jokob/2012	Retrospective	313	Melanoma	Metastatic	$>1 \times \text{ULN}$	2.75 (0.0001)	–	–
Neuman/2008	Prospective	589	Melanoma	Metastatic	200	1.42 (0.01)	–	–
Schmidt/2005	Fase II	321	Melanoma	Metastatic	$>1 \times \text{ULN}$	2.8 (0.001)	–	–
Schmidt/2007	Fase III	348	Melanoma	Metastatic	$>2 \times \text{ULN}$	2.2 (0.001)	1.6 (0.01)	–
Soubrane/2005	Retrospective	125	Melanoma	Metastatic	480	1.682 (0.0098)	–	–
Staudt/2010	Retrospective	265	Melanoma	Metastatic	$>1 \times \text{ULN}$	2.7 (0.001)	–	–
Weide/2012	Prospective	586	Melanoma	Metastatic	$>1 \times \text{ULN}$	1.6 (0.001)	–	–
Wevers/2013	Retrospective	119	Melanoma	IIIB-C	250	–	–	1.1 (0.75)
Gray/2012	Retrospective	44	Melanoma	Metastatic	per 100 IU/L increment	1.44 (0.001)	1.29 (0.002)	–
Donskov/2006	Prospective	120	mRCC	Metastatic	$>1 \times \text{ULN}$	3.1 (0.002)	–	–
Lagerwaard/1999	Retrospective	1292	Brain metastasis	Metastatic	350	1.55 (0.001)	–	–
Pinato/2014	Retrospective	118	Solid malignancies	Advanced or metastatic	450	3.2 (0.005)	3.11 (0.009)	–
Trédan/2011	Prospective	299	Solid malignancies	Advanced or metastatic	600	1.6 (0.0045)	–	–
Trivanovic'/2009	Prospective	145	Unknown primary site	Metastatic	$>1.25 \times \text{ULN}$	2.21 (0.001)	–	–
González-Billalabeitia/2009	Retrospective	66	Osteosarcoma	Localised extremity	$>1 \times \text{ULN}$	9.38 (0.009)	8.62 (0.009)	–
Armstrong/2013	Phase II	201	Prostate	Metastatic	204	2.68 ( $<0.001$ )	0.75 (0.288)	–

(Continued)

Supplementary Table I.(Continued)

Author/year	Type of study	No. pts	Disease site	Disease stage	Cut-off for LDH	OS HR (p.)	PFS HR (p.)	DFS HR
Coumans/2010	Prospective	179	Prostate	Hormone-refractory	174–228 229–313 314	0.84 (NR) 0.76 (NR) 1.9 (nr)	– – –	– – –
D’Amico/2005	Phase II	494	Prostate	Hormone-refractory	NR	3.1 (<0.0001) <sup>a</sup> 2.4 (0.001) <sup>b</sup>	– –	– –
Ferraldeschi/2008	Retrospective	144	Prostate	Hormone-refractory	NR	1.59 (0.048)	–	–
George/2005	Retrospective	191	Prostate	Hormone-refractory	199	1.28 (0.1122)	–	–
Halaby/2014	Retrospective	1050	Prostate	Metastatic	>1×ULN	1.40 (NR)	–	–
Humphrey/2006	Retrospective	171	Prostate	Metastatic	208	1.369 (0.0664)	–	–
Kume/2011	Retrospective	51	Prostate	Corticosteroid-refractory	237	1.43 (0.0742)	–	–
Narita/2012	Fase II	35	Prostate	Castration-resistant	193	6.084 (0.007)	–	–
Omlin/2013	Retrospective	442	Prostate	Metastatic	NR	1.51(0.014)	–	–
Saito/2007	Retrospective	241	Prostate	Metastatic	400	1.619 (0.0409)	–	–
Sher/2009	Retrospective	153	Prostate	Metastatic	NR	6.44 (0.0001)	–	–
Sonpavde/2014	Retrospective	847	Prostate	Metastatic	NR	2.86 (0.001)	–	–
Taplin/2005	Retrospective	321	Prostate	Hormone-refractory	208.5	1.583 (0.0001)	–	–
Templeton/2014	Retrospective	215	Prostate	Metastatic	>1.2×ULN	2.52 (0.001)	–	–
Yamada/2011	Retrospective	104	Prostate	Metastatic	>1×ULN	2.465 (0.0207)	–	–
Abel/2011	Retrospective	75	Renal	Metastatic	>1×ULN	2.42 (NR)	–	–
Amato/2014	Retrospective	57	Renal	Metastatic	>1.5×ULN	6.75 (0.001)	–	–
Armstrong/2012	Fase III	416	Renal	Metastatic	1.3	2.81 (0.001)	–	–
Atkinson/2014	Retrospective	185	Renal	Metastatic	927	3.05 (0.001)	2.42 (0.005)	–
Atzpodien/2003	Retrospective	425	Renal	Metastatic	220	1.3 (0.02)	–	–
Cetin/2014	Retrospective	59	Renal	Metastatic	>1×ULN	2.228 (0.032)	–	–
Culp/2010	Retrospective	566	Renal	Metastatic	618	1.66 (0.001)	–	–
Escudier/2007	Fase III	300	Renal	Metastatic	>1.5×ULN	1.681 (0.006)	–	–
Kamba/2014	Retrospective	144	Renal	Metastatic	>1.5×ULN	3.24 (0.035)	–	–
Patil/2011	Fase III	750	Renal	Metastatic	NR	2.009 (<0.001) and 1.797 (0.001) <sup>c</sup>	1.575 (0.003) and 1.553 (0.016) <sup>c</sup>	–
Peccatori/2005	Prospective	70	Renal	Advanced or metastatic	>1×ULN	2.43 (0.02)	–	–
Richey/2011	Retrospective	188	Renal	Metastatic	>1×ULN	1.55 (0.023)	–	–
Vermaat/2010	Retrospective	114	Renal	Metastatic	>1.5×ULN	3.6 (0.00073)	–	–
Zhang/2011	Retrospective	83	Renal	Metastatic	315	–	0.799 (0.455)	–
Fossa/1997	Retrospective	303	Seminoma	Advanced or metastatic	>2×ULN	–	3.58 (0.01)	–
Gerlinger/2010	Retrospective	117	GCTs	Metastatic	>1×ULN	3.4 (0.001)	3.7 (0.001)	–
Powles/2013	Retrospective	184	Seminoma	Metastatic	>1.5×ULN	–	1.93 (0.041)	–

DFS, disease-free survival; ED, extended disease; HR, hazard ratio; LD, limited disease; LDH, lactate dehydrogenase; MPM, malignant pleural mesothelioma; mRCC, metastatic renal cell carcinoma; NEC, neuroendocrine carcinoma; N<sup>o</sup>, number; NPC, nasopharyngeal carcinoma; NSCLC, non-small cell lung cancer; OS, overall survival; PFS, progression-free survival; pts, patients; SCLC, small cell lung cancer; ULN, upper limit of normal. <sup>a</sup>281 patients in validation cohort; <sup>b</sup>213 patients in study cohort; <sup>c</sup>for sunitinib and interferon patients arms, respectively.



Supplementary Figure 1. Study-level ( $n = 34$  trials) association of the cut-off used to define cut-off of LDH concentration and the hazard ratio for overall survival. Each study is represented by a circle, and the area of the circle is proportional to the number of patients enrolled in each study. The gradient of the line represents the results of the meta-regression ( $p = 0.11$ ).