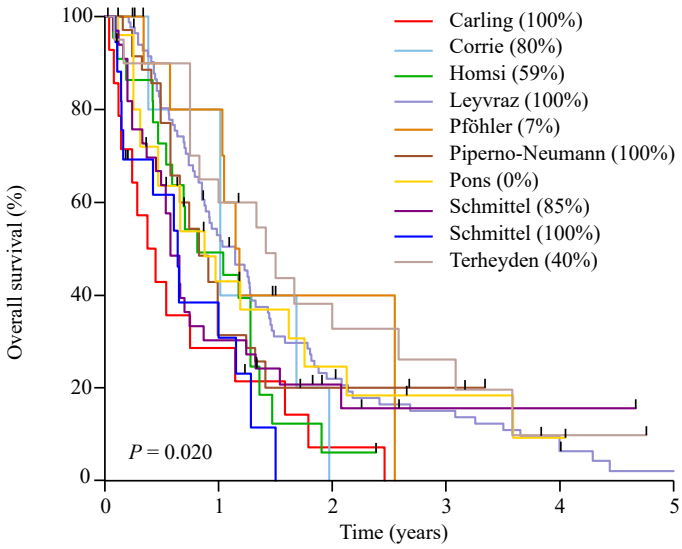
Supplemental digital content 4.pdf - Supplemental figures

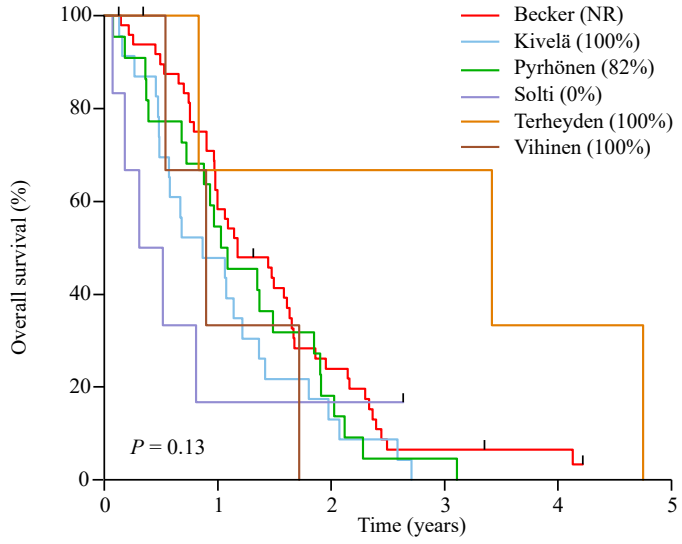
A. Conventional chemotherapy (CHT)



Number at risk

Carling [1]	14	4	1	0	0	0
Corrie [2]	5	4	0	0	0	0
Homsi [3]	22	10	1	0	0	0
Leyvraz [4]	85	42	17	11	3	1
Pföhler [5]	14	8	1	0	0	0
Piperno-Neumann [6]	35	11	4	1	0	0
Pons [7]	25	8	4	2	1	0
Schmittel [9]	33	10	4	1	1	0
Schmittel [8]	19	4	0	0	0	0
Terheyden [10]	20	13	7	4	1	0

B. Chemoimmunotherapy (CIT)

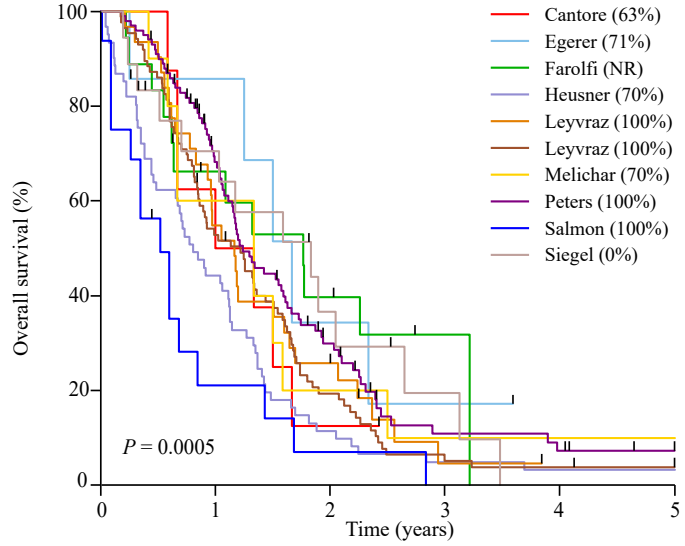


Number at risk

Becker [11]	48	29	11	3	2	0
Kivelä [12]	24	11	3	0	0	0
Pyrhönen[13]	22	12	4	1	0	0
Solti [14]	6	1	1	0	0	0
Terheyden [15]	3	2	2	2	1	0
Vihinen [16]	4	1	0	0	0	0

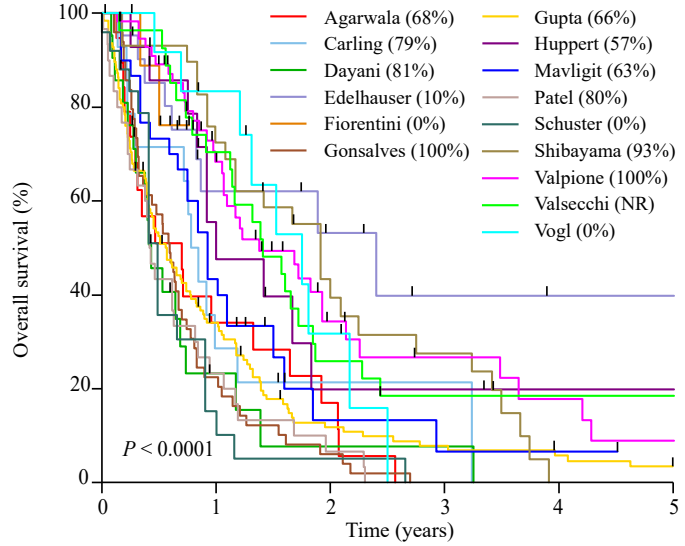
Fig. S1. Kaplan-Meier plots (A-M) of overall survival after metastatic uveal melanoma by treatment modality, digitised data for each individual study to display heterogeneity. The spread of the survival curves that derives from differences in study design, inclusion criteria, and case mix may be viewed as an empiric representation of a confidence interval for each modality. The percentage within brackets refers to first-line treatments. *P* values were calculated by log-rank test. Abbreviations: NR not reported.

C. Hepatic intra-arterial chemotherapy (HIA)



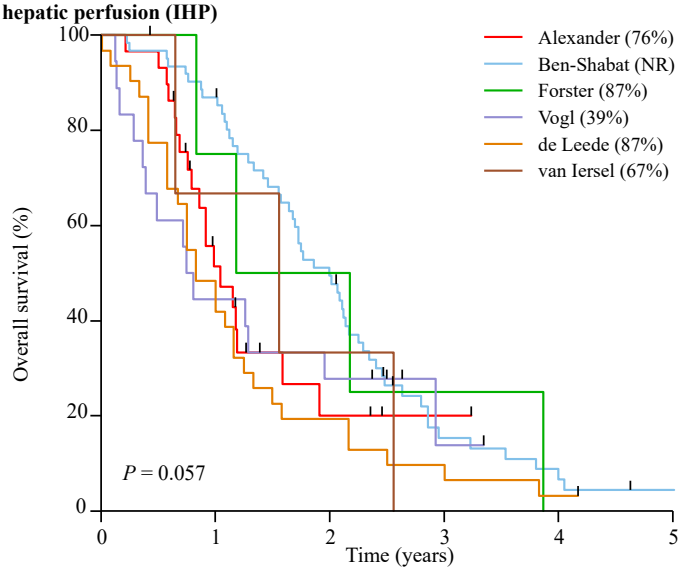
Number at risk						
Cantore [17]	8	5	1	0	0	0
Egerer [18]	7	5	2	1	0	0
Farolfi [19]	18	10	6	1	0	0
Heusner [20]	61	27	7	3	2	2
Leyvraz [21]	31	17	7	1	0	0
Leyvraz [4]	86	43	15	5	3	0
Melichar [22]	10	6	2	1	1	1
Peters [25]	100	58	22	6	4	0
Salmon [23]	16	3	1	0	0	0
Siegel [24]	18	11	5	2	0	0

D. Transarterial chemoembolisation (TACE)



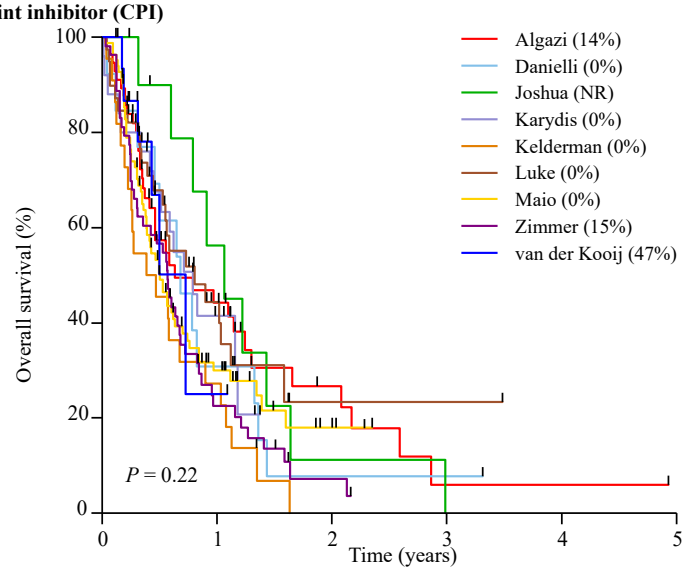
Number at risk						
Agarwala [26]	19	6	3	0	0	0
Carling [1]	14	4	1	1	0	0
Dayani [27]	21	3	1	1	0	0
Edelhauser [28]	21	9	5	2	1	1
Fiorentini [29]	10	0	0	0	0	0
Gonsalves [30]	49	11	3	0	0	0
Gupta [31]	125	39	12	8	5	0
Huppert [32]	14	7	2	2	1	1
Mavligit [33]	30	13	2	1	1	0
Patel [34]	30	7	2	0	0	0
Schuster [35]	25	3	1	0	0	0
Shibayama [36]	29	21	11	7	0	0
Valpione [37]	58	29	10	6	4	2
Valsecchi [38]	27	19	7	4	4	4
Vogl [39]	12	9	3	0	0	0

E. Isolated hepatic perfusion (IHP)



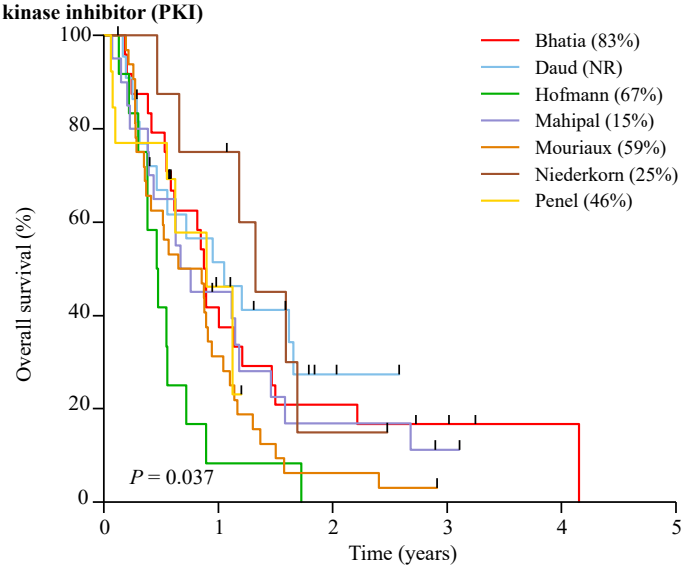
Number at risk						
Alexander [40]	29	12	3	1	0	0
Ben-Shabat [41]	61	51	29	7	4	1
Forster [43]	5	3	2	1	0	0
Vogl [45]	18	8	5	1	0	0
de Leede [42]	31	15	6	3	1	0
van Iersel [44]	3	2	1	0	0	0

F. Checkpoint inhibitor (CPI)



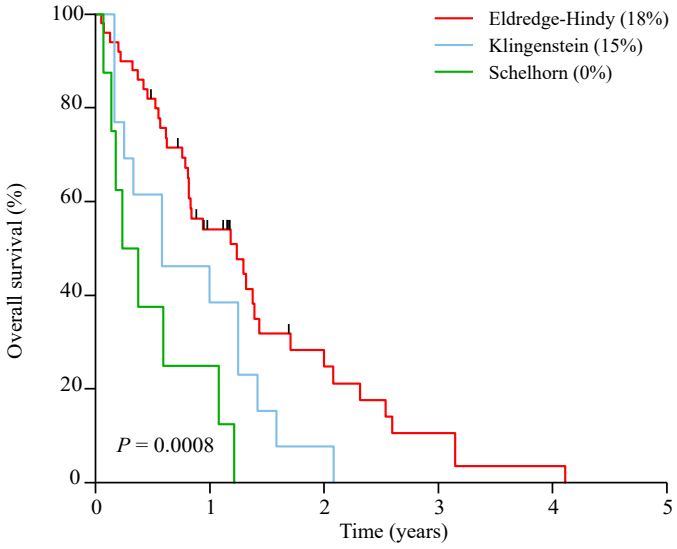
Number at risk						
Algazi [46]	56	17	6	1	1	0
Danielli [47]	13	4	1	1	0	0
Joshua [48]	11	5	1	0	0	0
Karydis [49]	25	6	0	0	0	0
Kelderman [50]	22	6	0	0	0	0
Luke [51]	39	10	1	1	0	0
Maio [52]	82	17	2	0	0	0
Zimmer [54]	53	10	2	0	0	0
van der Kooij [53]	17	1	0	0	0	0

G. Protein kinase inhibitor (PKI)



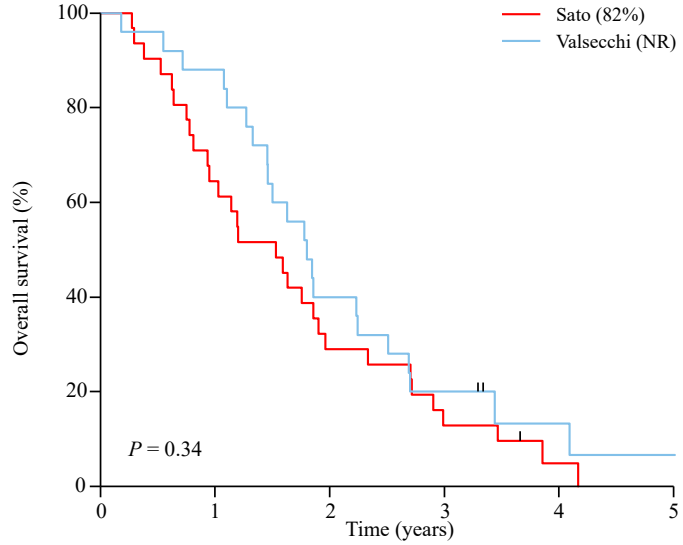
Number at risk						
Bhatia [55]	24	10	5	3	1	0
Daud [56]	23	10	2	0	0	0
Hofmann [57]	12	1	0	0	0	0
Mahipal [58]	20	8	3	1	0	0
Mouriaux [59]	32	10	2	0	0	0
Niederkorn [60]	8	6	1	0	0	0
Penel [61]	13	3	0	0	0	0

H. Selective internal radiation therapy (SIRT)



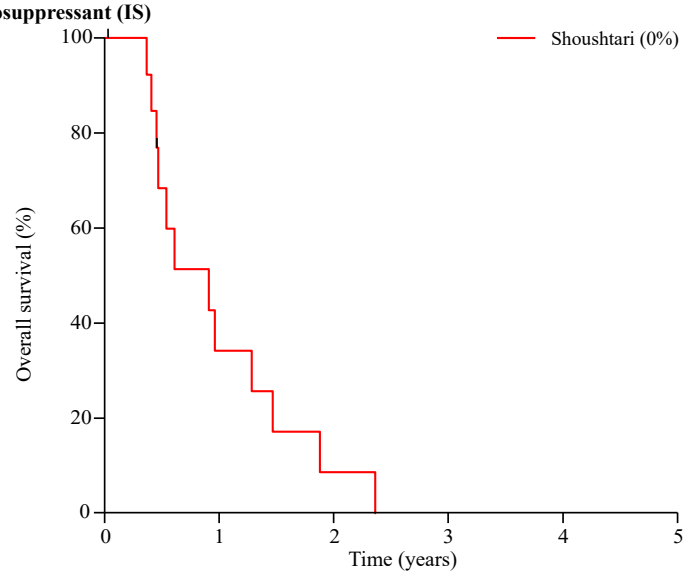
Number at risk						
Eldredge-Hindy [62]	50	22	7	3	1	0
Klingenstein [63]	13	6	1	0	0	0
Schelhorn [64]	8	2	0	0	0	0

I. Immunoembolisation (IE)



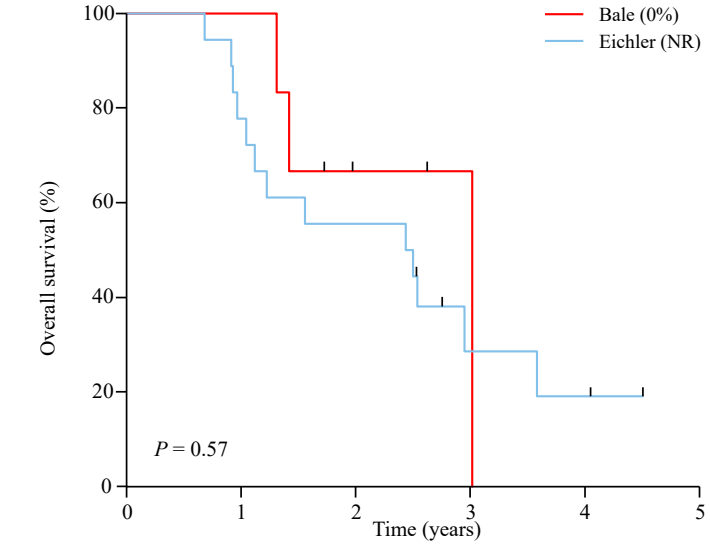
Number at risk						
Sato [65]	31	20	9	4	1	0
Valsecchi [38]	25	22	10	5	2	1

J. Immunosuppressant (IS)



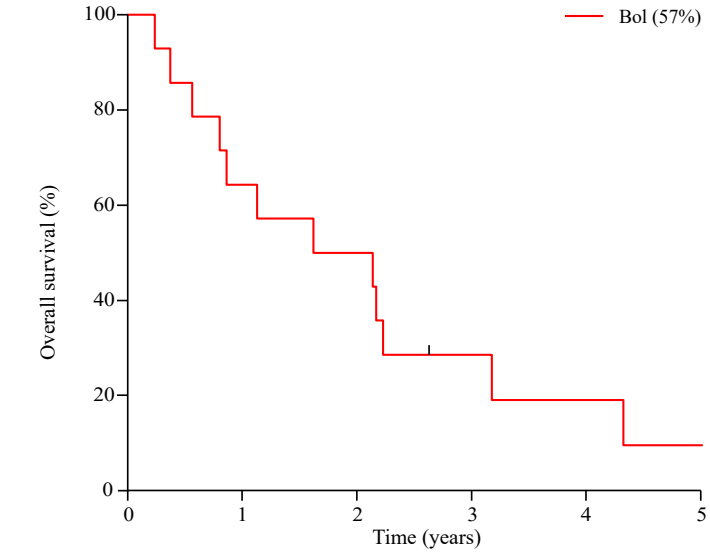
Number at risk						
Shoushtari [66]	14	4	1	0	0	0

K. Liver-directed thermotherapy (LDT)



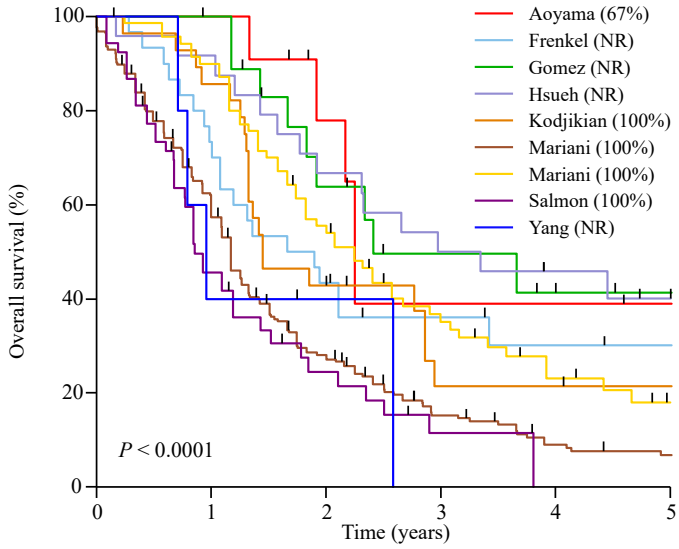
Number at risk						
Bale [67]	6	6	2	1	0	0
Eichler [68]	18	14	10	3	2	0

L. Vaccine

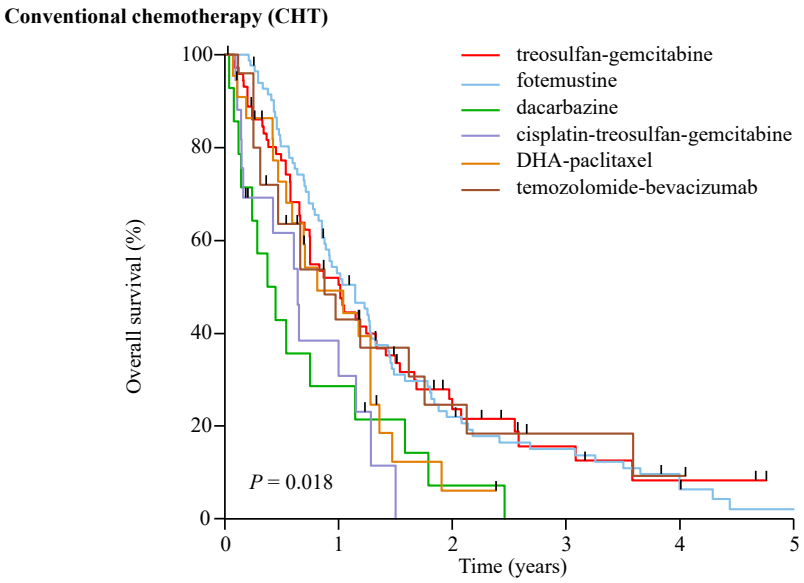


Number at risk						
Bol [69]	14	9	7	3	2	1

M. Surgery



Number at risk						
Aoyama [70]	12	11	6	3	3	2
Frenkel [71]	35	22	13	8	5	4
Gomez [72]	18	18	10	6	3	2
Hsueh [73]	24	22	16	12	8	0
Kodjikian [74,75]	28	24	9	4	4	3
Mariani [77]	255	144	59	24	13	8
Mariani [76]	70	63	38	21	10	1
Salmon [23]	53	23	8	3	0	0
Yang [78]	5	2	1	0	0	0

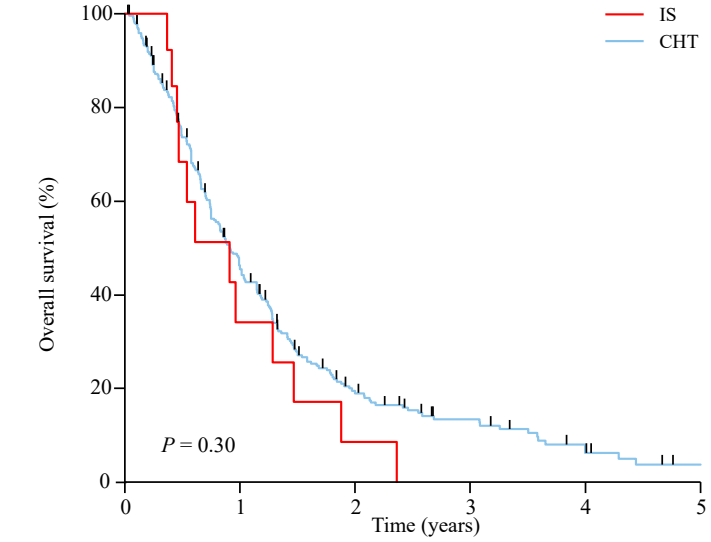


Number at risk

treosulfan-gemcitabine [2,5,9,10]	72	35	12	5	2	0
fotemustine [4]	85	42	17	11	3	1
dacarbazine [1]	14	4	1	0	0	0
cisplatin-treosulfan-gemcitabine [8]	19	4	0	0	0	0
DHA-paclitaxel [3]	22	10	1	0	0	0
temozolomide-bevacizumab [6]	25	8	4	2	1	0

Fig. S2. Kaplan-Meier plot of overall survival after metastatic uveal melanoma by conventional chemotherapy agents, digitised data for each individual study to display heterogeneity. The spread of the survival curves that derives from differences in study design, inclusion criteria, and case mix may be viewed as an empiric representation of a confidence interval. *P* value was calculated by log-rank test.

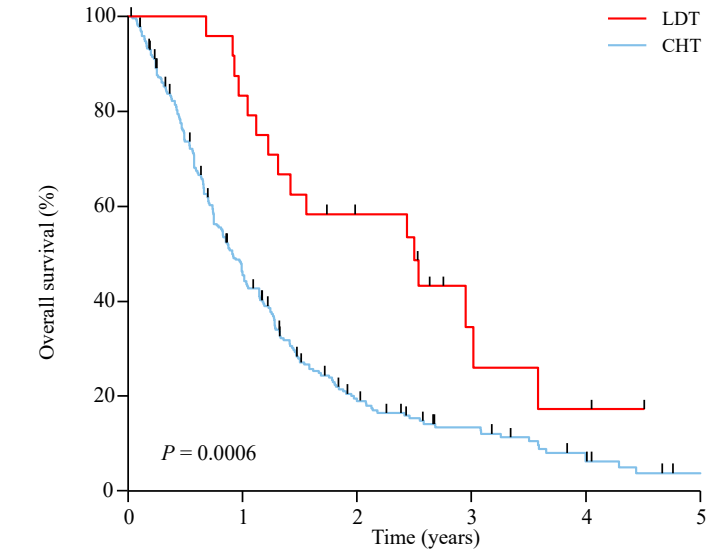
A. IS vs CHT



Number at risk

CHT	272	114	39	19	6	1
IS	14	4	1	0	0	0

B. LDT vs CHT

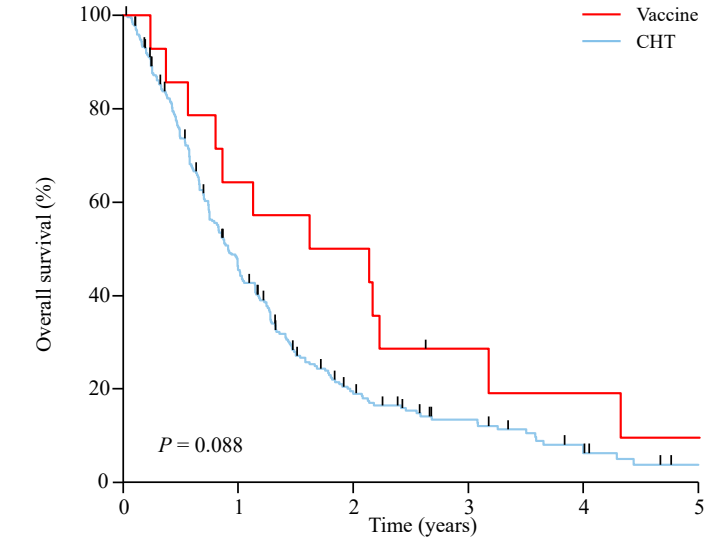


Number at risk

CHT	272	114	39	19	6	1
LDT	24	20	12	4	2	0

Fig. S3. Kaplan-Meier plots (A-D) of overall survival after metastatic uveal melanoma, pooled data for each treatment modality administered to fewer than 50 patients, compared against conventional chemotherapy. *P* values were calculated by log-rank test.
Abbreviations: CHT, conventional chemotherapy; IS, immunosuppressant; LDT, liver-directed thermotherapy.

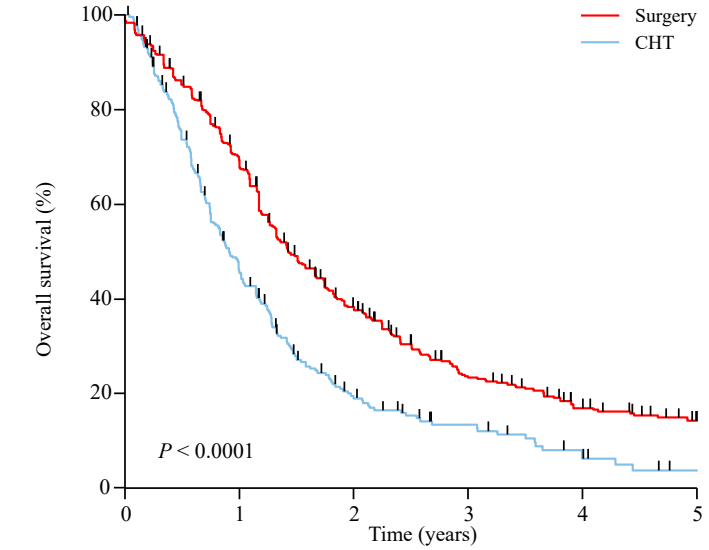
C. Vaccine vs CHT



Number at risk

CHT	272	114	39	19	6	1
Vaccine	14	9	7	3	2	1

D. Surgery vs CHT



Number at risk

CHT	272	114	39	19	6	1
Surgery	500	329	160	81	46	20

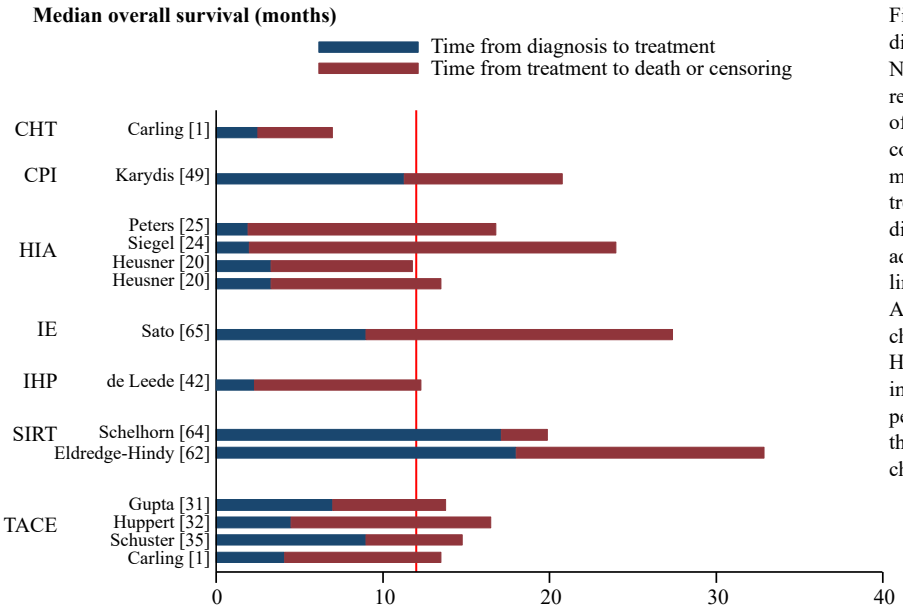
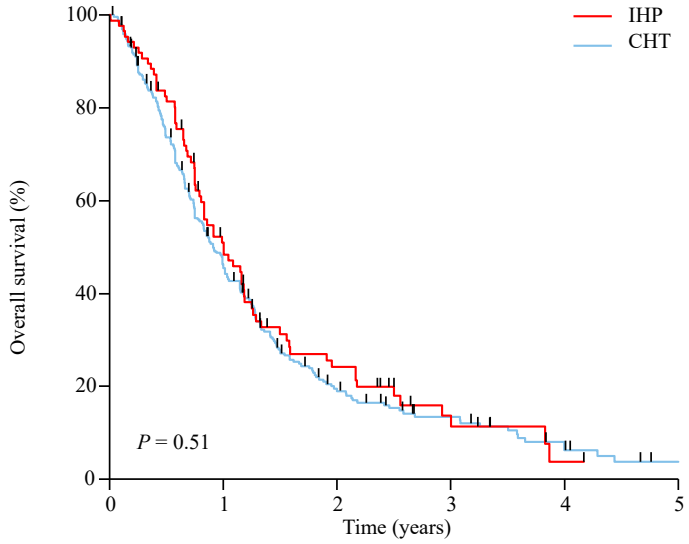


Fig. S4. Components of overall survival from diagnosis of metastasis to death or censoring. Note that the majority of studies would have reported a median overall survival in excess of 12 months (vertical red line) should one consider survival from diagnosis of metastases rather than from initiation of study treatment. The highly variable interval from diagnosis to treatment is a source of bias in addition to the variable percentage of first-line treatments in many reports. Abbreviations: CHT, conventional chemotherapy; CPI, checkpoint inhibitor; HIA, hepatic intra-arterial chemotherapy; IE, immunoembolisation; IHP, isolated hepatic perfusion; SIRT, selective internal radiation therapy; TACE, transarterial chemoembolisation.

IHP vs CHT without Ben-Shabat et al. [41]

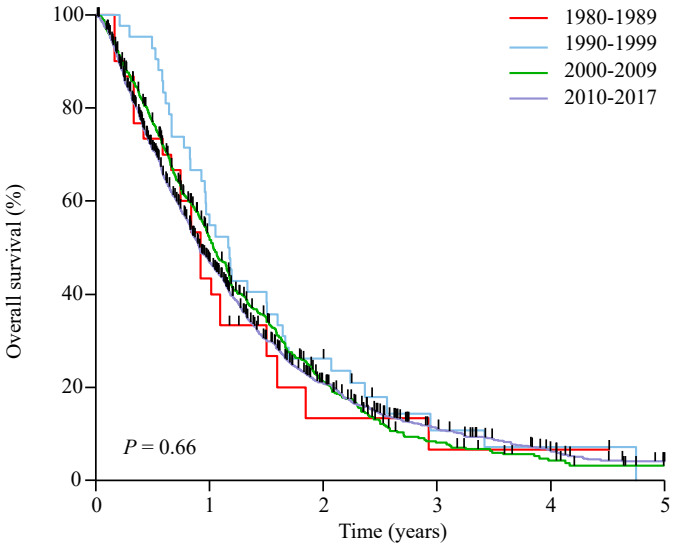


Number at risk

CHT	272	114	39	19	6	1
IHP	86	40	17	6	1	0

Fig. S5. Kaplan-Meier plot of overall survival after metastatic uveal melanoma, pooled data for isolated hepatic perfusion without article [41] against conventional chemotherapy. P-value was calculated by log-rank test. Abbreviations: CHT, conventional chemotherapy; IHP, isolated hepatic perfusion.

Overall survival by decade

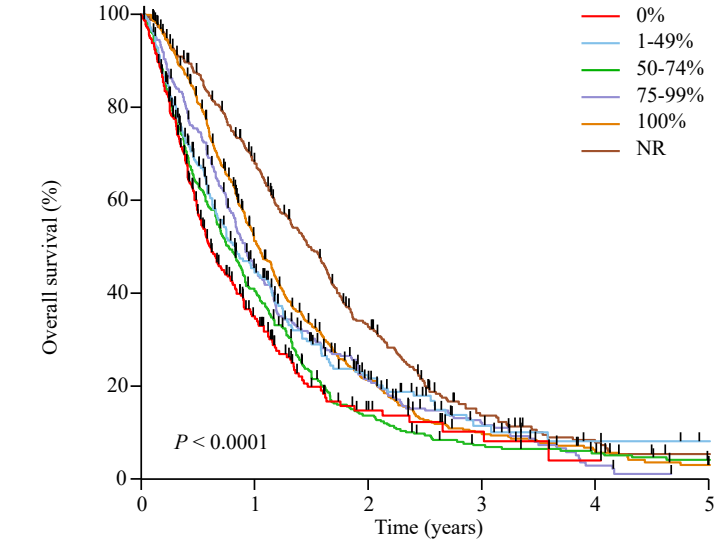


Number at risk

1980-1989	30	13	2	1	1	0
1990-1999	42	24	10	3	1	0
2000-2009	519	236	84	25	10	1
2010-2017	1403	582	214	87	38	14

Fig. S6. Kaplan-Meier plots (A-B) of overall survival after metastatic uveal melanoma, pooled data by decade. All treatment modalities were included except for surgery. *P* value was calculated by log-rank test for trend.

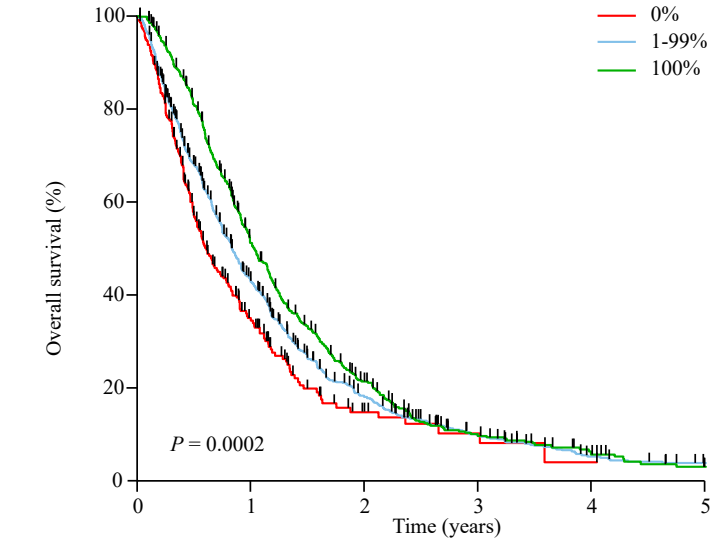
A. Overall survival by percentage of first-line treatments



Number at risk

0%	275	67	13	5	1	0
1-49%	253	89	31	9	3	1
50-74%	357	140	42	19	12	5
75-99%	269	117	48	23	4	0
100%	510	232	84	32	15	3
NR	330	210	92	28	15	6

B. Overall survival by percentage of first-line treatments



Number at risk

0%	275	67	13	5	1	0
1-99%	879	346	121	51	19	6
100%	510	232	84	32	15	3

Fig. S7. Kaplan-Meier plots (A-B) of overall survival after metastatic uveal melanoma, pooled data by percentage of first-line treatments. All treatment modalities were included except for surgery. *P* values were calculated by log-rank test for trend. Abbreviation: NR, not reported (curve not included when calculating the *P* value).

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