

Supplementary material

Appendix Table 1: Probability of relapse (both locoregional and distant)

	IA		IB		IIA				III				III tr		Systemic relapse for patients with a locoregional relapse	
	% Relapse	Probabi lity	% Relapse	Probability	% Relapse	Probabil ity	% Relapse	Probability	% Relapse	Probabili ty	% Relapse	Probability	% Relapse	Probabili ty	% Relapse	Probability
1-year	0.0	0.000	5.0	0.050	25.0	0.250	25.0	0.250	55.0	0.250	53.0	0.530	72.0	0.720	42.0	0.445
5-year	6.0	0.017	22.9	0.059	44.9	0.090	60.8	0.215	79.0	0.303	100.0	0.758	100.0	0.588	100.0	0.445
10-year	7.5	0.004	29.5	0.021	49.9	0.023	65.5	0.033	85.7	0.167	100.0	NA	100.0	NA	100.0	NA
15-year	11.0	0.009	34.1	0.017	52.1	0.010	67.8	0.022	85.7	0.000	100.0	NA	100.0	NA	100.0	NA
20-year	13.5	0.007	34.1	0.000	60.7	0.060	67.8	0.000	89.3	0.242	100.0	NA	100.0	NA	100.0	NA

Source: Table 3, Bernengo ²⁶; Figure 1, Romano ²⁷. Annual probabilities were interpolated between 1 to 5 years, 5 to 10 years, 10 to 15 years and 15 to 20 years.

Appendix Table 2: Stage-specific probabilities for the site of first relapse.

	Locoregional relapse	Distant relapse	Source
Stage I	0.847	0.153	Table 2, Bernengo ²⁶
Stage II	0.865	0.135	
Stage III	0.490	0.510	Table 2, Romano ²⁷

Sites of first relapse for stages I and II were obtained from the total number of satellite/in-transit nodes and relapses in soft tissue and viscera.

Appendix Table 3: Medical-therapy specific probabilities of first relapse.

	Dabrafenib + Trametinib		Vemurafenib + Cobimetinib		Nivolumab		Pembrolizumab	
	%	Probability	%	Probability	%	Probability	%	Probability
1-year	51.0	0.510	53.0	0.530	59.0	0.590	48.0	0.480
5-year	100.0	0.751	100.0	0.441	100.0	0.307	100.0	0.689
10-year	100.0	NA	100.0	NA	100.0	NA	100.0	NA
15-year	100.0	NA	100.0	NA	100.0	NA	100.0	NA
20-year	100.0	NA	100.0	NA	100.0	NA	100.0	NA

Appendix Table 4: Medical-therapy-specific probabilities of death due to melanoma.

	Dabrafenib + Trametinib		Vemurafenib + Cobimetinib		Nivolumab		Pembrolizumab	
	%	Probability	%	Probability	%	Probability	%	Probability
1-year	27.0	0.270	25.0	0.250	27.0	0.270	26.7	0.267
5-year	95.4	0.206	95.4	0.206	95.4	0.206	95.4	0.206
10-year	100.0	0.206	100.0	0.206	100.0	0.206	100.0	0.206
15-year	100.0	NA	100.0	NA	100.0	NA	100.0	NA
20-year	100.0	NA	100.0	NA	100.0	NA	100.0	NA

Appendix Table 5: Stage at diagnosis probabilities.

	Melanoma not detected by screening ^a (%)	Parameters of the Dirichlet distribution	True positive on screening ^b (%)	Parameters of the Dirichlet distribution
Stage 0	21.60	367	30.36	516
Stage I	53.75	914	55.42	942
Stage II	11.30	192	4.80	82
Stage III	6.16	105	4.00	68
Stage IV	1.71	29	1.53	26
Regression	5.48	93	3.89	66

^a Personal communication from the Veneto Cancer Registry. Applied to the no-screening branch as well as to patients in the screening branch who failed to attend or were false negative cases.

^b Probabilities are obtained based on the per cent of relative variation observed before and after implementing the SCREEN project in Germany.²⁰

Appendix Table 6: Screening costs.

	Unit cost (€)	Unit of measurement for a hypothetical 100,000 target population ^a	Total cost (€)
Mail invitation	0.10	100,000 people	10,000
Remuneration for GP trainers per hour	100.00	9.2 hours ^b	921
Out-of-hours service per hour	32.00	95.7 hours ^c	3,061
Total-body-skin-examination by GPs	15.00	19,000 examination	285,000
Dermatologist examination	20.50	3,175 examination	65,086
Skin punch biopsy for melanoma	27.60	5.3 biopsies ^d	146
Excisional skin biopsy for primary melanoma	39.05	206.5 biopsies	8,062
Total cost (€)			372,277

^a Point estimates based on the hypotheses described in the section 'Screening strategy' and reported in Table 1.

^b 8-hour course for every 30 GPs (34.5 GPs per 100,000 target population).

^c 34.5 GPs per 100,000 target population. 12-hour shift every 4.33 (6,500/1,500) GPs. 6,500 and 1,500 are the mean numbers of patients cared for by out-of-hours doctors and GPs, respectively.

^d Total number of biopsies: 212 (see Table 1). Punch and excisional biopsies account for 2.5% and 97.5% of total biopsies, respectively (source: Buja et al. ⁸).

Appendix Table 7: Initial and follow-up costs for each stage.

	Initial costs (€) (includes diagnosis, stadiation and surgery)	Follow-up/year for stable patients (€) (includes follow-up exams and medical therapy)
0	134	14
IA	1,809	48
Regression	1,990	97
IB	1,946	225
IIA	1,948	347
IIB	2,430	801
IIC	2,347	1,830
III	7,816	8,390
III TR	1,121	35,992
IV	2,317	63,436