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# Long-term Survival of Patients With Invasive Ultra-thin Cutaneous Melanoma

## *A Single-center Retrospective Analysis*

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**Abstract:** The incidence of cutaneous melanoma is increasing worldwide, especially for thin melanoma (Breslow  $\leq 1$  mm). Thin cutaneous melanoma has a favorable prognosis but there are few data about the prognosis of patients with ultra-thin cutaneous melanoma (Breslow  $\leq 0.5$  mm). Our aim was to investigate the disease-free survival among patients with invasive cutaneous melanoma with Breslow  $\leq 0.5$  mm after 10 years from the initial diagnosis.

A retrospective review of 240 cutaneous melanoma patients with Breslow  $\leq 0.5$  mm was performed. Recurrence, death from cutaneous melanoma, and disease-free survival were all identified.

In the whole group of patients, we observed only 2 deaths from cutaneous melanoma. Median follow-up was 13, 11 years. Among all 240 patients, 221 were alive and disease free, 2 died of cutaneous melanoma, 11 died of other non-neoplastic diseases, 5 died of other neoplastic diseases different from melanoma, and 1 patient had a local recurrence; therefore the 10-year melanoma survival rate was 99.6%.

Our data indicate that death from cutaneous melanoma in the group of patients with Breslow  $\leq 0.5$  mm was a very rare event and that diagnosis at this stage dramatically decreases the risk of developing metastatic tumors to a  $<0.5\%$  also after a 10-year period of follow-up. Limitation of the study includes the fact that other risk factors for melanoma, notably ulceration, and mitotic rate, were not evaluated.

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**Abbreviations:** AJCC = American Joint Committee on Cancer, CM = cutaneous melanoma.

## INTRODUCTION

Cutaneous melanoma (CM) is a severe type of skin malignancy and is responsible for the majority of skin cancer death.<sup>1</sup> The incidence of this tumor is increasing worldwide especially in the fair-skinned populations. CM incidence has been steadily increasing since the mid 1960s and is predicted to

continue increasing for at least 2 more decades. However, this trend is associated with a reduction in median tumor thickness according to Breslow depth of invasion<sup>2-5</sup> and patients with thin CM represent  $\sim 70\%$  of the new cases.<sup>1,6</sup> The increased frequency of thin melanoma in recent decades may be explained by an easier access to skin cancer screening clinics, but also by an overdiagnosis of melanoma by pathologists.

According to both the American Joint Committee on Cancer (AJCC) and the guideline on the diagnosis and treatment of CM of the European Dermatology Forum, malignant lesions with a Breslow  $\leq 1.0$  mm are considered “thin” melanoma.<sup>7,8</sup> Breslow tumor thickness is one of the most important histological prognostic factors for primary CM. In the absence of other risk factors (such as ulceration and/or mitotic rate  $>1/\text{mm}^2$ ) thin CM presents a good survival rate. The 10-year melanoma survival rate for thin CM ranges from 82% to 97%.<sup>1,6,8,9</sup>

There are several epidemiological studies concerning the prognosis at both 5- and 10-year of thin CM<sup>10,11</sup> whereas prognostic studies in patients with Breslow  $\leq 0.5$  mm (“ultra-thin CM”) have rarely been conducted. The aim of this study was to analyze the survival rate of patient with invasive CM with a Breslow  $\leq 0.5$  mm after 10 years of follow-up in order to more accurately predict the prognosis of patients with very thin CM. The data of our study may provide a more accurate risk stratification of patients with thin melanoma, which could improve both follow-up strategy and clinician-patient communication after the diagnosis of a thin melanoma.

## PATIENTS AND METHODS

A retrospective review of 240 patients diagnosed with single invasive very thin CM was carried out. We identified all subjects with a new diagnosis of very thin CM in the period 1989 to 2004 followed-up for at least 10 years at the Melanoma and Soft Tissue Sarcoma Unit of the Veneto Institute of Oncology. Therefore, patients lost to follow-up before their 10-year visit were not included in the study. The population in this area is mainly Caucasian and fair-skinned. The treatment of these patients affected by CM with Breslow  $\leq 0.5$  mm consisted of diagnostic excision with 1- to 2-mm margins followed by wider excision to achieve histologically confirmed 1-cm margins in healthy tissue. Recurrence, death from melanoma, and disease free survival rates were all identified. Other prognostic factors, such as mitotic rate, were not investigated because they were not available for all study patients. Data was obtained for diagnosis, staging, and follow-up of the patients; therefore, the need for institutional review board approval was waived by the local ethics committee for this study. No informed consent was obtained from the patients, given the retrospective nature of the study.

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**TABLE 1.** Distribution of Patients According to Breslow Depth of Invasion

Melanoma Thickness in mm (Breslow Depth)	Number of Patients
0.01–0.09	4
0.091–0.15	9
0.151–0.2	15
0.201–0.25	29
0.251–0.3	35
0.301–0.35	34
0.351–0.4	43
0.401–0.45	44
0.451–0.5	27
Total	240

**RESULTS**

The total number of newly diagnosed invasive ultra-thin CM in the period 1989 to 2004 with a follow-up evaluation for at least 10 years was 240 (88 men and 152 women). Median follow-up was 13, 11 years. Table 1 depicts details on Breslow thickness of newly diagnosed invasive ultra-thin CM. Table 2 shows that, after a follow up of at least 10 years, a total of 221 patients were alive and disease free, 2 died of CM, 11 died of other non-neoplastic diseases, 5 died of other neoplastic diseases different from CM, and 1 patient had a local recurrence; therefore the survival rate for CM death at 10-year follow-up was 99.6%. Table 3 shows other clinical-pathological characteristics of the patients investigated whereas Table 4 includes details of the 2 patients deceased for melanoma.

**DISCUSSION**

The incidence of CM is increasing and the preponderance of CMs diagnosed today are “thin” in terms of Breslow criteria.<sup>3,12</sup> About 40 years ago, it was realized that CMs could be divided into categories with better or worse prognosis through the use of prognostic models. The first simple model (Clark levels of invasion and Breslow thickness) is still in use; in the current AJCC classification other 2 tumor-associated factors have been recognized for thin melanomas: mitotic rate and ulceration, nonetheless thickness remains the single most useful variable.<sup>7</sup>

**TABLE 2.** Distribution of Patients According to Their Current Status

Currents Status	Number of Patients	Number of Patients
	Absolute Frequency	Relative Frequency
Alive and disease free	221	0.92
Died of melanoma	2	0.008
Died of other non-neoplastic diseases	11	0.045
Died of other neoplastic diseases different from melanoma	5	0.02
Local recurrence	1	0.004
Total	240	1

**TABLE 3.** Additional Patient and Tumor Characteristics

Sex	
Male	88
Female	152
Ulceration	
Not determined	27
Absent	205
Present	8
Clark level	
Not determined	4
II	149
III	84
IV	3
Mitosis	
Not determined	44
<1	190
≥1	6
Location	
Not determined	4
Head and neck	10
Trunk	117
Superior limb	36
Inferior limb	73

Very few studies have evaluated the long-term prognosis of patients with invasive CM showing a Breslow  $\leq 0.5$  mm. Maurichi et al<sup>4</sup> have investigated in a multicenter study the overall survival in patients with thin melanoma; they showed that the 12-year overall survival of 803 patients with ultra-thin CM was 96.8%. Einwachter et al<sup>13</sup> investigated 428 patients with CM  $\leq 0.5$  mm thick followed-up for a minimum of 5 years. For the whole group, only 3 patients died for melanoma, but all 3 of these deaths occurred in patients who subsequently developed further thicker primary CM.

The purpose of our study was to analyze the prognosis of patients with invasive CM with Breslow  $\leq 0.5$  mm after at least 10 years of follow-up from the initial diagnosis. Patients were selected on the basis of at least 10 years of follow-up as several recurrences develop  $>5$  years after diagnosis, and often 8 to 10 years later.<sup>4</sup> In general, melanoma recurrence 10 years after the initial diagnosis is very rare; however, late recurrences are observed, and they seem more common in patients with thin primary lesions.<sup>4</sup> In our study, only 2 patient deaths in the whole group were attributed to the primary CM. Of the 2 patient deaths attributed to CM, 1 patient died after 16 years of follow-up and the other patient after 2 years from the initial diagnosis. Our study is the first single-center investigation of invasive

**TABLE 4.** Clinical-Pathological Characteristics of the 2 Deceased Patients

Age	68	73
Sex	Male	Male
Years of follow-up	2	16
Mitotic rate	Not determined	Not determined
Ulceration	Absent	Absent
Breslow thickness	0.43	0.3
Location	Trunk	Trunk
Clark level	III	II

ultra-thin CM with a follow-up of at least 10 years and provides the longest median follow-up of this group of patients. These data indicate that patients with ultra-thin CMs are at extremely low risk for systemic spread. This may have some practical implications in relation to staging investigations and follow-up of patients. Moreover, the diagnosis of CM creates intense fear in patients which contrasts with the extremely good prognosis of ultra-thin CM. Therefore these data can be utilized by clinicians in order to reassure patients that the disease is highly unlikely to spread and affect their survival. Limitations of the study were the lack of correlation with other risk factor parameters, in particular, ulceration and mitotic rate.

In conclusion our data indicate that death from CM in the group of patients with Breslow  $\leq 0.5$  mm was a very rare event and that diagnosis at this stage dramatically decreases the risk of developing metastatic tumors to a  $<0.5\%$  also after a 10-year period of follow-up.

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