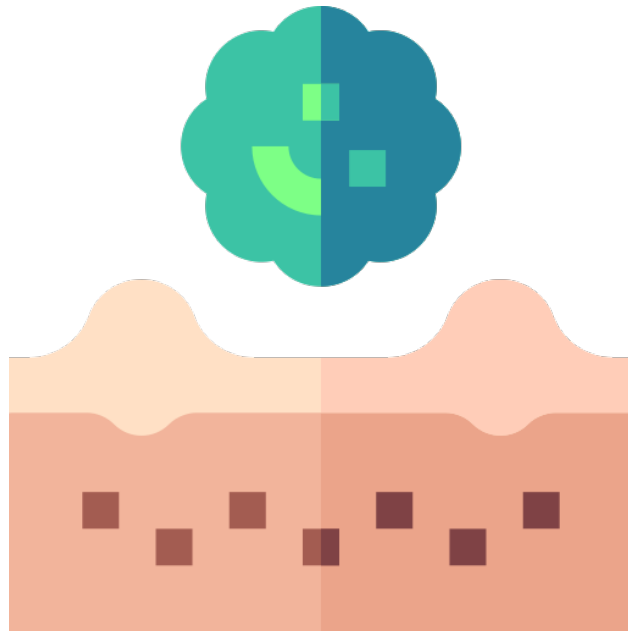


# Immuno- & targeted therapy saving melanoma patient lives



## CASE OUTLINE

### I. Case for change

- *Situation*
- *Challenge*
- *Paradigm shift*
- *Patient population*

### II. Value to patients

### III. Value to the healthcare system

### IV. Value to society

### V. Annex

- *Key assumptions*
- *Reference list*

# Case summary | Melanoma

## Immuno- & targeted therapy saving melanoma patient lives

### CASE FOR CHANGE



- **Situation** – Melanoma is a type of skin cancer of growing public health concern. Melanoma represents 4% of all skin cancers cases; however, it is responsible for 80% of all skin cancer deaths. This means melanoma is the most dangerous type of skin cancer. If left untreated, melanoma is deadly in most cases
- **Challenge** – Before 2011, there was no scientifically proven effective treatment for patients in stage III and IV melanoma. Therefore, survival rates were extremely low
- **Paradigm shift** – Since 2011, several immunotherapies and targeted therapies against stage III and IV melanoma were introduced in the EU27, providing the opportunity to treat melanoma, and extending life expectancy of melanoma patients significantly
- **Population** – EU27 incidence of melanoma has steadily increased over several decades. In 2020, over 116k men and women were diagnosed with melanoma. On average, 9% and 6% percent of melanoma patients have stage III and IV disease at diagnosis, respectively. However, incidence and stage distribution vary among EU countries

### VALUE FOR PATIENTS



- **Preventable deaths** – Between 2011 and 2022, the survival rate for patients with stage IV melanoma has more than doubled (based on Dutch survival rates). The introduction of immunotherapies and targeted therapies against stage III and IV melanoma has reduced the number of patients dying from the disease in the first 5 years after diagnosis.

### VALUE TO THE HEALTHCARE SYSTEM



- *There is limited evidence supporting an increase in value for the healthcare system from a monetary and resource use perspective related to the introduction of innovation for melanoma. The introduction of immunotherapy and targeted therapy is mainly associated with an increase in costs and resource use compared to the situation before 2011, as there were no viable treatment options back then. As such we propose to focus on value for patients and society in this case.*

### VALUE TO SOCIETY



- **Reducing absenteeism** – Immunotherapies and targeted therapies increases the number of people employed after treatment for stage III and IV melanoma. Improved work productivity due to immunotherapies and targeted therapies against stage III and IV melanoma translates to productivity and labour income of 3.8 M working hours and €391 M, respectively.

### TOWARDS THE FUTURE



- **Selecting patients that benefit** – While immuno- and targeted therapies improved the lives of many melanoma patients, high unmet needs remain for a subset of patients. Improved diagnostics will enable better selection of patient groups that will benefit from immunotherapies and/ or targeted therapies. Melanoma patients who will not benefit from immunotherapies and targeted therapies therefore will not be at risk of developing unnecessary side effects.

# Melanoma is a growing public health concern and the most dangerous type of skin cancer, representing 4% of all skin cancers and 80% of skin cancer deaths



Melanoma



In 2020, over **106,000 patients were diagnosed with melanoma** in EU27<sup>1</sup>. The incidence of melanoma has steadily increased over the past decades<sup>1</sup> and is expected to continue to grow with another 13.7% by 2040, to nearly 121,000 diagnoses per year



Melanoma is the **6<sup>th</sup> most frequently occurring cancer** in EU27<sup>1</sup>



Melanoma occurs in **older and younger people**<sup>1</sup>

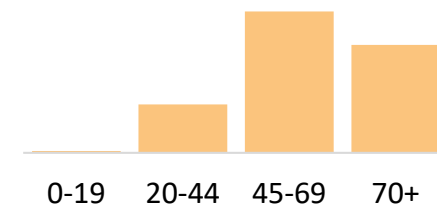


Melanoma is the **most dangerous type of skin cancer**. It represents only 4% of all skin cancer case, but 80% of all skin cancer deaths in Europe<sup>3</sup>

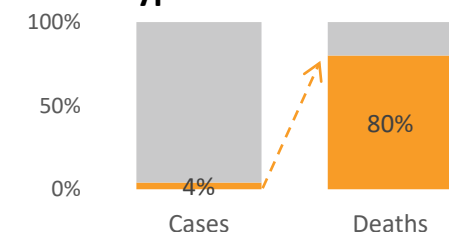


In 2020, **nearly 16,000 people died from melanoma** in EU27<sup>1</sup>

Estimated distribution of age at diagnosis<sup>1</sup>



Melanoma is the **most dangerous type of skin cancer**<sup>3</sup>

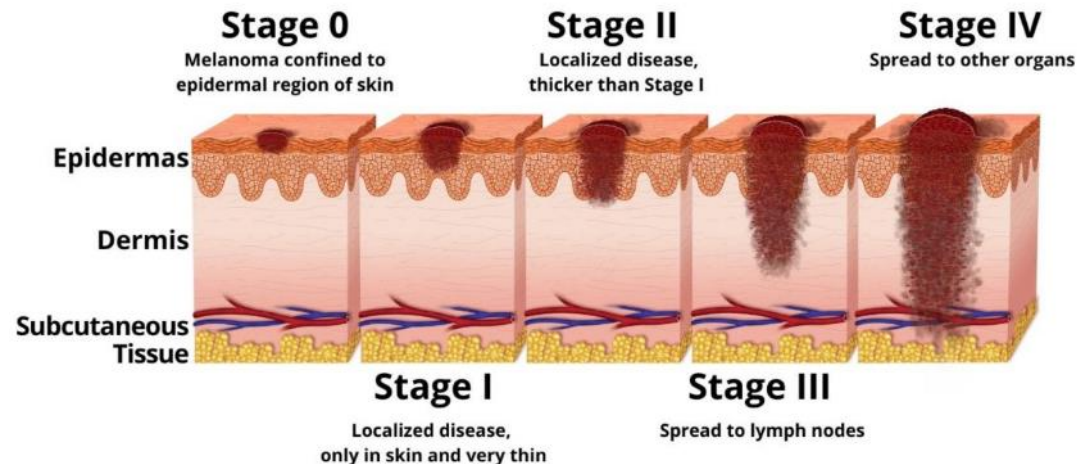


Melanoma: 4% of all skin cancer cases but 80% of skin cancer deaths

1. EUROPEAN UNION, 2021  
2. EUROPEAN COMMISSION 2022  
3. ESMO MELANOMA ESSENTIALS FOR CLINICIANS CHAPTER 1

# Disease severity greatly depends on the stage of the disease, with a high unmet need for stage III and IV patients: no treatment available before 2011

## Stages of melanoma<sup>1</sup>



*“There is no doubt that ten years ago we were not able to treat stage IV melanoma. We had 7-8% 5-year survival, for stage IV. It was horrible.”*

– Dermato-oncologist and professor of cutaneous oncology

## Stages of melanoma



There are **five stage of melanoma (0–IV)**, each divided in up to four subgroups (a–d) that indicate a higher risk within each stage

## Stages 0–II<sup>2</sup>



**Stages 0–II** are typically **treated with wide excision** (surgery to remove the melanoma and a margin of normal skin around it)

## Stages III and IV<sup>2</sup>



Stage III / IV melanoma (unresectable or metastatic melanoma) patients had a poor prognosis. **No scientifically proven effective treatment for stage III / IV** was available before 2011<sup>3</sup>

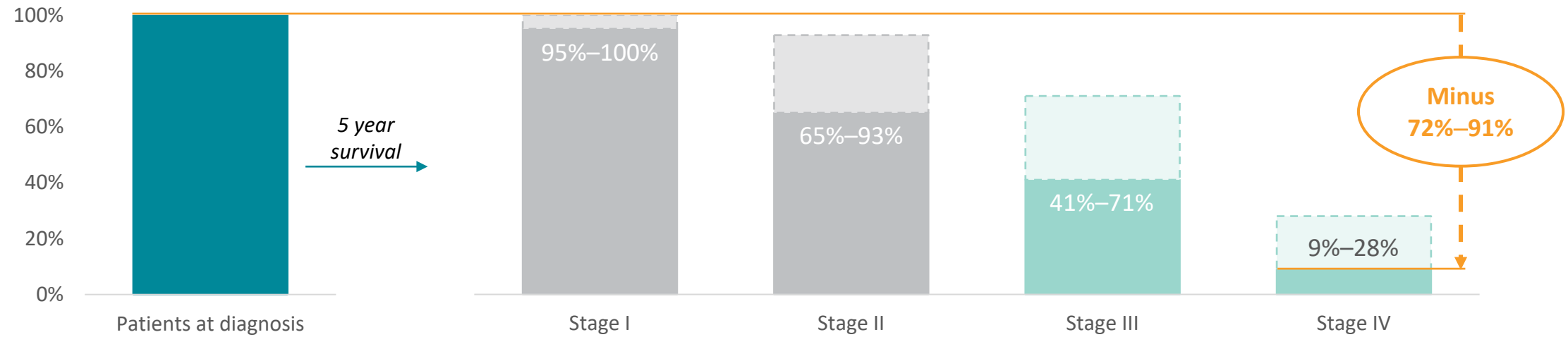
*“With many other cancers, you could always hope that there would be something there that would treat it. But with melanoma, up until 2011, there was absolutely nothing.”*

– Gillian Nuttal, CEO Melanoma UK

1. [HTTPS://WWW.AIMATMELANOMA.ORG/STAGES-OF-MELANOMA/](https://www.aimatmelanoma.org/stages-of-melanoma/)  
2. AMERICAN CANCER SOCIETY, ACCESSED AUGUST 2022  
3. INTERVIEW WITH HEALTHCARE PROFESSIONAL

# Without effective treatment, late stage melanoma survival rates are extremely low. Only 1–3 out of 10 stage IV patients survived 5 years after diagnosis pre 2011

5-year survival rate before introduction of immuno- and targeted therapies<sup>1</sup>



Stage III and IV melanoma **severely impacted** the **lives of patients** and their **friends and family**, as chances of survival were slim and no treatment was available

*“Back then, certainly in the UK, we had absolutely nothing that treated melanoma. All that a patient would be offered in a stage III / IV setting would be radiotherapy or the old fashion chemotherapies. But clinicians and patients knew it was relatively unsuccessful in melanoma. A patient would have a 3-9 months life expectancy, which was a real tough situation to face for people. [...] From a patient point of view, it was absolutely such a blow to have nothing that could treat it [melanoma].”*

– Gillian Nuttal, CEO Melanoma UK

# We estimate that, in 2020, around 15.7k patients were newly diagnosed with stage III or IV melanoma in EU27

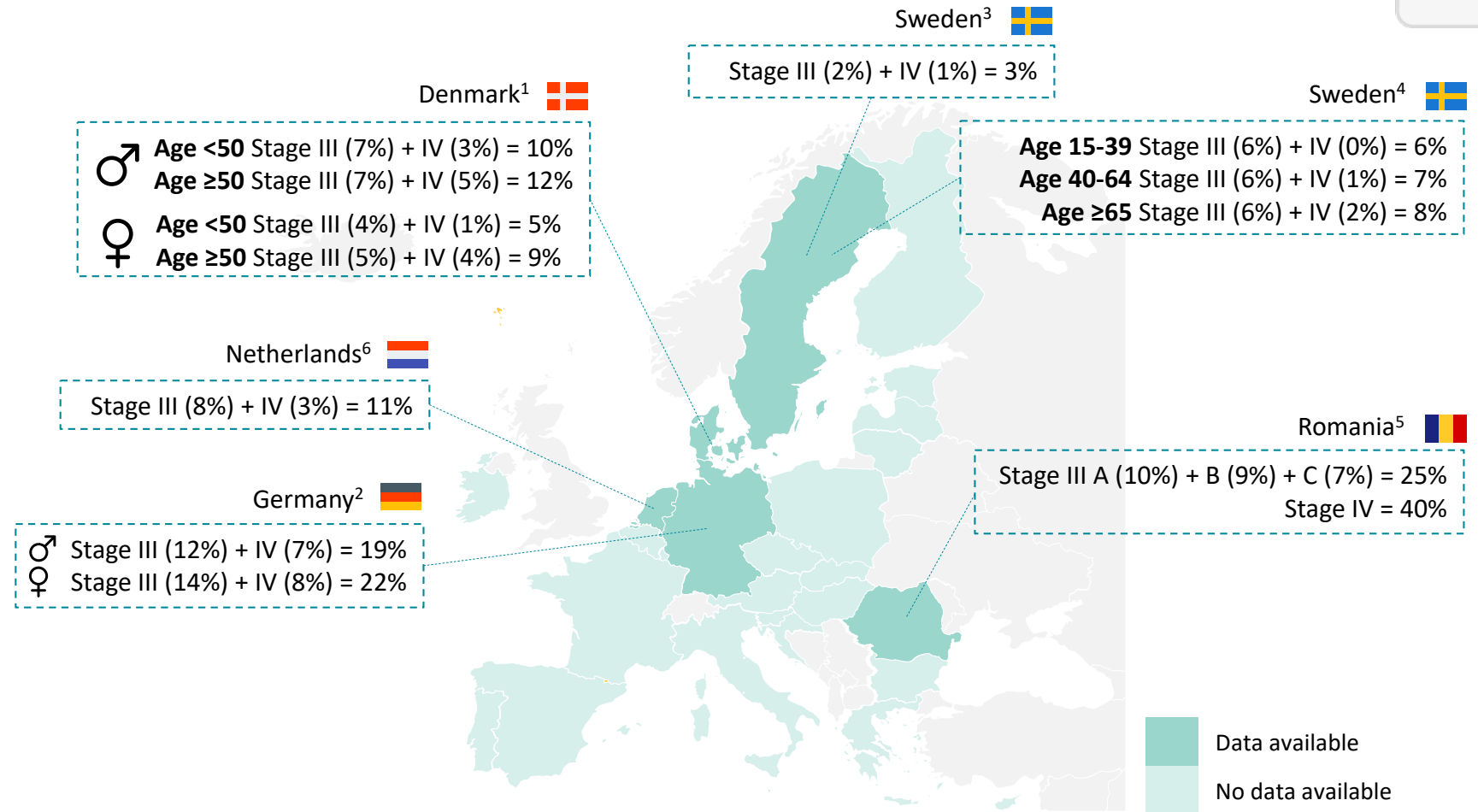
Distribution of patients amongst the various stages varies by country. This is due to the variety in screening and diagnosis. If countries focus on early diagnosis, relatively more patients are diagnosed in the early stages of the disease, preventing progression into later stages.

Information about the distribution of patients amongst stages is available only for a limited number of countries.

On the basis of studies from these countries, the average distribution of patients is:

- Stage III: **9% of patients**
- Stage IV: **6% of patients**

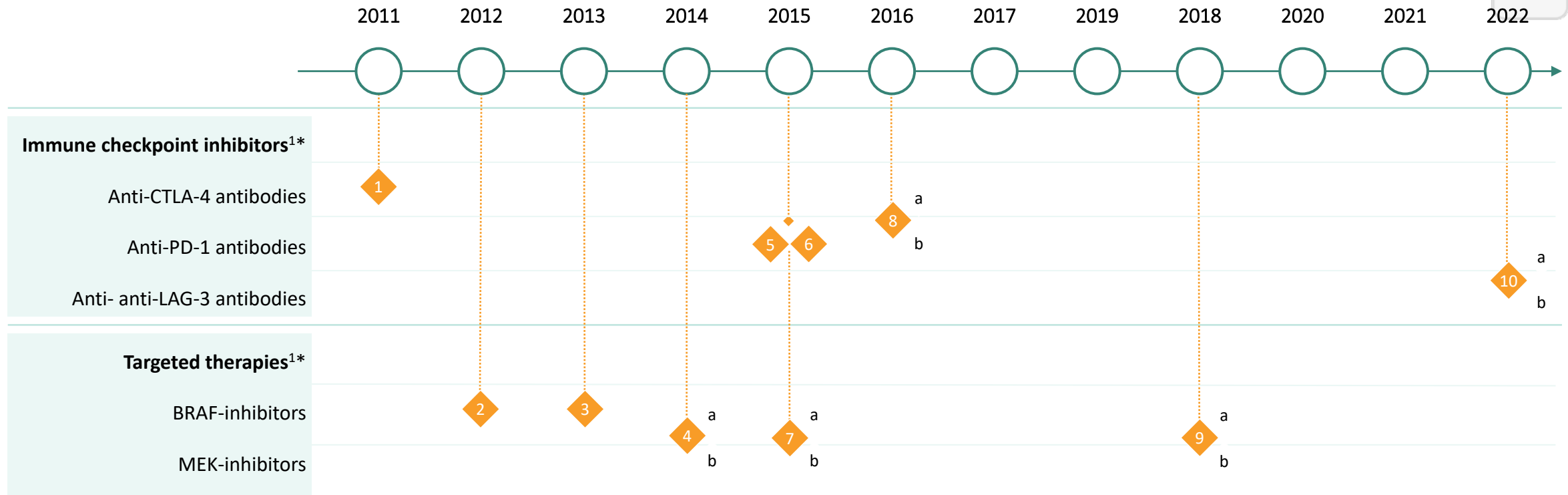
Unmet need for  
**~15,700 new patients per year**



Countries where information is available about the distribution of patients amongst the various disease stages

1. BAY ET AL. 2015  
 2. EISEMANN ET AL. 2012  
 3. ERIKSSON ET AL. 2013  
 4. PLYM ET AL. 2014  
 5. ROTARU ET AL. 2019  
 6. LEENEMAN ET AL. 2021

# In 2011, the outlook for stage III and IV patients completely changed, with the introduction of several immuno- and targeted therapies\*



*“The dominant conversation in my clinic was about palliative care. That is what I was talking about to most patients. [...] And today, I’m in a situation to talk to people about Standard of Care options, which represent therapies with high level of benefit.”*

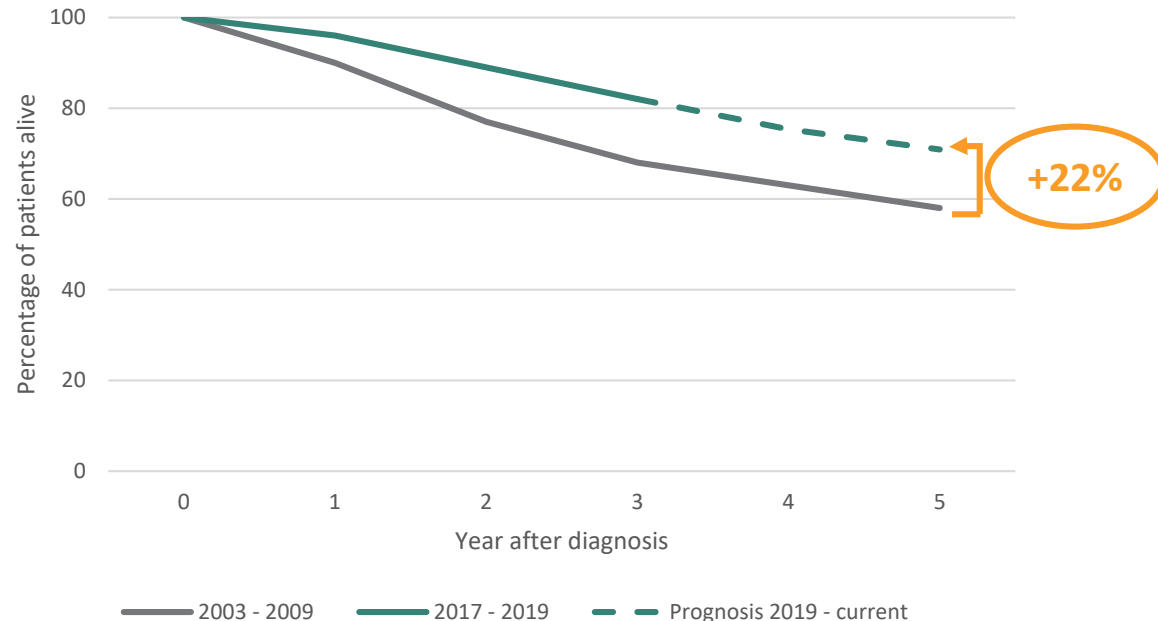
– Medical Oncologist and Cancer Researcher

\* A / B INDICATE COMBINATION THERAPIES  
1. EUROPEAN MEDICINES AGENCY, ACCESSED AUGUST 2022

# In the Netherlands, 5-year survival rates for stage III and IV melanoma have increased by 22% and 120%, respectively

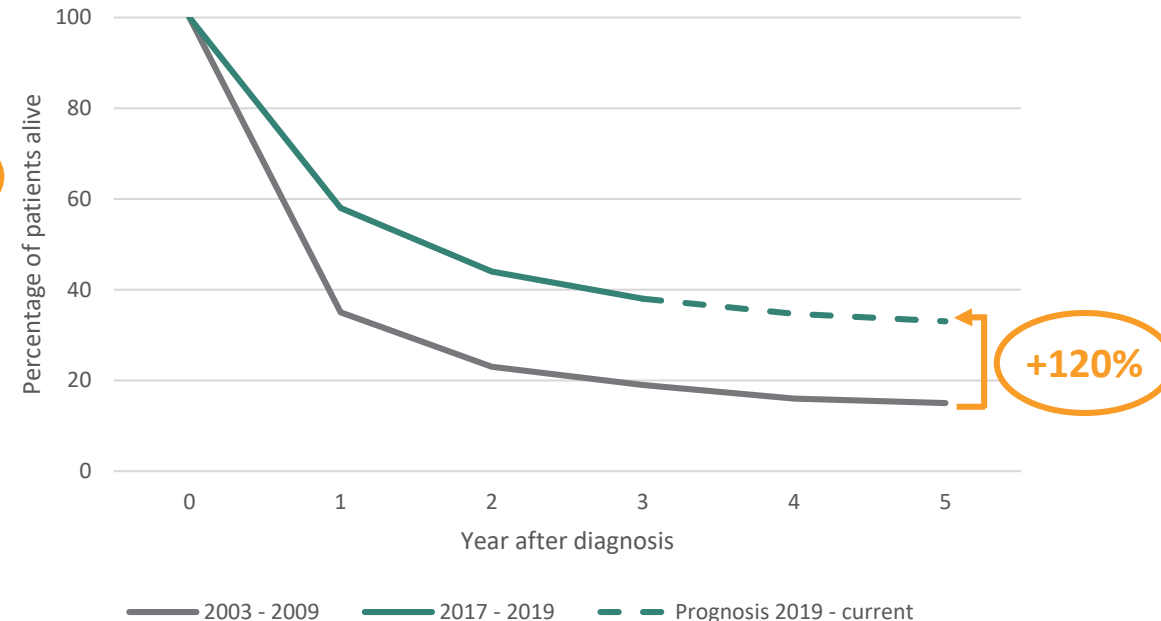
## Stage III melanoma

The 5-year survival rate for stage III melanoma patients increased from 58% between 2003 and 2009 to 71% between 2019 and now<sup>1</sup>



## Stage IV melanoma

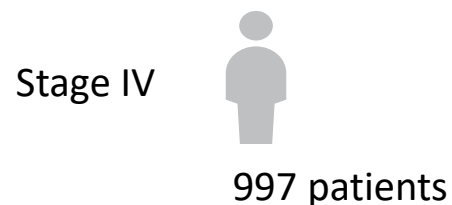
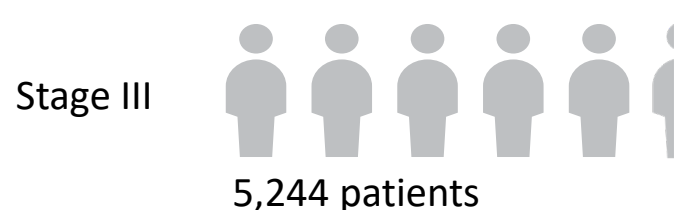
The 5-year survival rate for stage IV melanoma patients increased from 15% between 2003 and 2009 to 33% between 2019 and now<sup>1</sup>



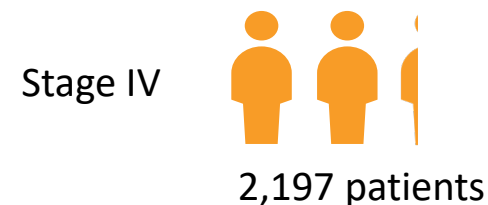
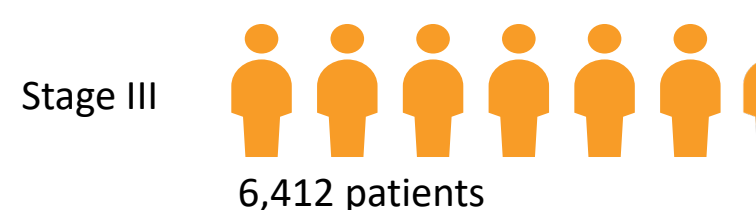


# 2368 more patients, of the 15.7k with stage III/IV, could be alive 5 years after their diagnosis if they are treated with immuno- and targeted therapies\*

**World without immuno- and targeted therapy for melanoma**  
(number of patients who are alive 5 years after diagnosis)\*\*



**World with immuno- and targeted therapy for melanoma**  
(number of patients who are alive 5 years after diagnosis)\*



*"In the course of 15 years, melanoma has evolved into being one of the most treatable metastatic cancers, today. That's astonishing."*  
– Medical Oncologist and Cancer Researcher

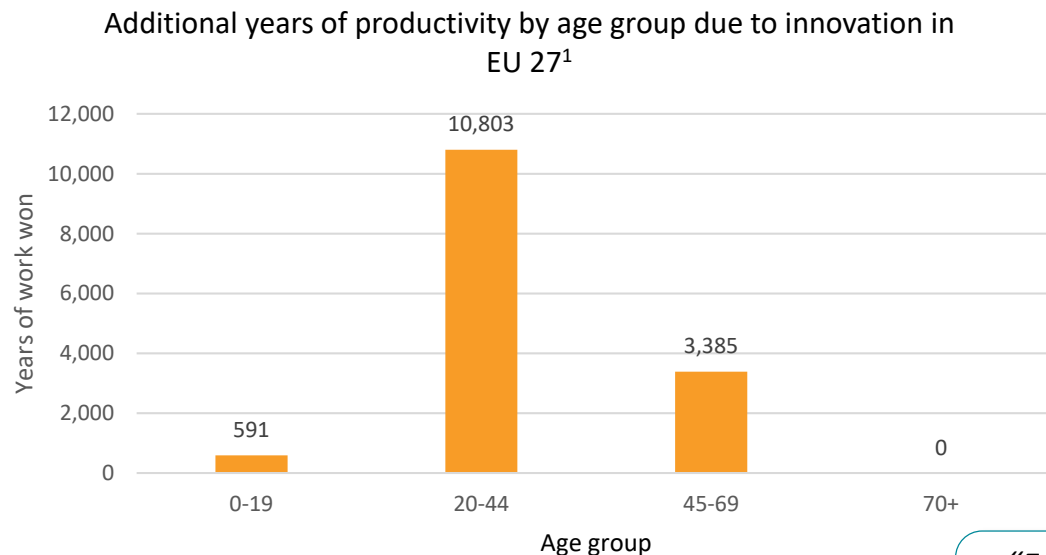
When patients achieve 5-year survival, their prognosis is good and relatively few patients die after 5 years. Treatment with immuno- and targeted therapies results in **an additional 2,368 patients being alive after 5 years\*\*\***

\* ASSUMING THAT THE IMPROVED SURVIVAL RATES ARE ENTIRELY ATTRIBUTABLE TO IMMUNO- AND TARGETED THERAPIES  
\*\* CALCULATION ARE BASED ON A PROJECTION OF DUTCH SURVIVAL RATES ON EU27 INCIDENCE  
\*\*\* DUE TO THE RELATIVELY YOUNG AGE OF THE INNOVATION, THIS CANNOT YET BE CURED PATIENTS YET

# Improved work productivity due to the increase in survival rates for stage III and IV melanoma translates to 3.8M working hours and €391M income per year

## Increased survival leads to increased work productivity

Stage III and IV melanoma patients who reach 5-year survival usually resume or continue work. The number of years of work left depends on the patient's age



**Improved work productivity results in economic gain**  
Improved work productivity due to the increase in survival rates for stage III and IV melanoma results in:



Annual productivity in EU27 by<sup>1,2</sup>  
**+ 3.8M working hours**



Annual labour income in EU27<sup>1,2,3</sup>  
**+ €391M**

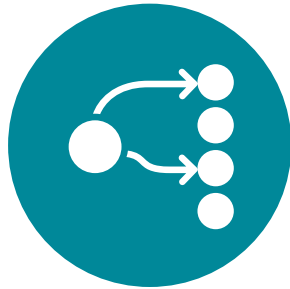
*“From a societal point of view, we lost the ability for that man [a relative that died from melanoma] to earn and to pay taxes.”*

– Gillian Nuttal, CEO Melanoma UK

1. EUROSTAT, UNEMPLOYMENT RATE. ACCESSED: AUGUST 2022  
2. EUROSTAT, AVERAGE WORKING HOURS. ACCESSED: AUGUST 2022  
3. EUROSTAT, ANNUAL EARNINGS. ACCESSED: AUGUST 2022

# While immuno- and targeted therapies improved the lives of many melanoma patients, high unmet need remains for a subset of patients

High unmet needs remain for patients who do not respond well to current treatment. This can be improved by focusing on:



## Improved treatment selection to increase efficacy

Via molecular diagnostics, to better match patient to treatment to improve efficacy<sup>1</sup>



## Improved understanding of tolerability

Via molecular diagnostics, to better understand the risk of adverse events by treatment<sup>2</sup>

*"[...] we give the immunotherapy agents to all comers. Roughly 50% of these patients will have long-term survival. We have no means to predict in advance who that 50% of patients will be."*

– Medical Oncologist and Cancer Researcher

# Assumptions for the Melanoma case study



## Distribution of patients amongst the various stages

- We based the distribution of patients amongst the various stages in EU27 on figures from Sweden, Denmark, Germany, Romania and the Netherlands. We calculated the (non-weighted) average from these countries. We assumed that the proportion of stage III and IV patients is the same for all age classes.

## Survival rates and additional patients being alive after 5 years

- Survival rates were based on data from the Netherlands
- Survival rates for 2019 to 2022 are not available yet. For these years, we have estimated the survival rates by extrapolating the trendline from the most recent available cohort (2010–2016) to the cohort of 2017–2019
- We are aware that other factors, like better screening, could have influenced the improvement in survival rates over the past years. However, we cannot single out the impact of each intervention that took place between 2011 (when the first new agent was approved by the EMA) and now. That is why we assume that the improved survival rates are entirely attributable to immuno- and targeted therapies
- To quantify the additional number of patients being alive after 5 years, we applied the difference of survival rates in the Netherlands to the incidence and stage distribution in EU27

## Economic gains

- We based these calculations on the additional 2,368 patients surviving 5-years after diagnoses
- We assumed that the mean hours of work in EU27 was the same for all age groups, for which we used 37.2 hours (2022)<sup>1</sup>
- We assumed that mean annual earnings in EU27 were the same for all age groups for, which we used €27,081 (2014, most recent available year)<sup>2</sup>
- We corrected for the mean unemployment rate in EU27, for which we used 6.2% (2022)<sup>3</sup>
- We assumed that every patient would work up and until the age of 65

1. EUROSTAT. ACCESSED: JULY 2022. LINK: [HTTP://APPSO.EUROSTAT.EC.EUROPA.EU/NUI/SUBMITVIEWTABLEACTION.DO3](http://appsso.eurostat.ec.europa.eu/nui/submitviewtableaction.do3)

2. EUROSTAT. ACCESSED: JULY 2022. LINK: [HTTPS://EC.EUROPA.EU/EUROSTAT/DATABROWSER/VIEW/EARN\\_SES\\_ANNUAL\\_CUSTOM\\_3021783/DEFAULT/TABLE?LANG=EN](https://ec.europa.eu/eurostat/databrowser/view/EARN_SES_ANNUAL_CUSTOM_3021783/DEFAULT/TABLE?LANG=EN)

3. EUROSTAT. DATE: 3 MAY 2022. LINK: [HTTPS://EC.EUROPA.EU/EUROSTAT/DOCUMENTS/2995521/14613608/3-03052022-AP-EN.PDF/36631A07-778C-EF80-01F2-8A052BDE985E?T=1651561306689#:~:TEXT=IN%20MARCH%202022%2C%20THE%20EURO,FROM%207.5%25%20IN%20MARCH%202021.2](https://ec.europa.eu/eurostat/documents/2995521/14613608/3-03052022-AP-EN.PDF/36631A07-778C-EF80-01F2-8A052BDE985E?T=1651561306689#:~:TEXT=IN%20MARCH%202022%2C%20THE%20EURO,FROM%207.5%25%20IN%20MARCH%202021.2)

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## Interviews

Interviews conducted in July and August 2022 with 1 Patient Expert and 2 Healthcare Professionals (KOLs).