MPNE conference

Date: March 21st-24th, 2019, Burussels

**MPNE 2019 Quickstart**

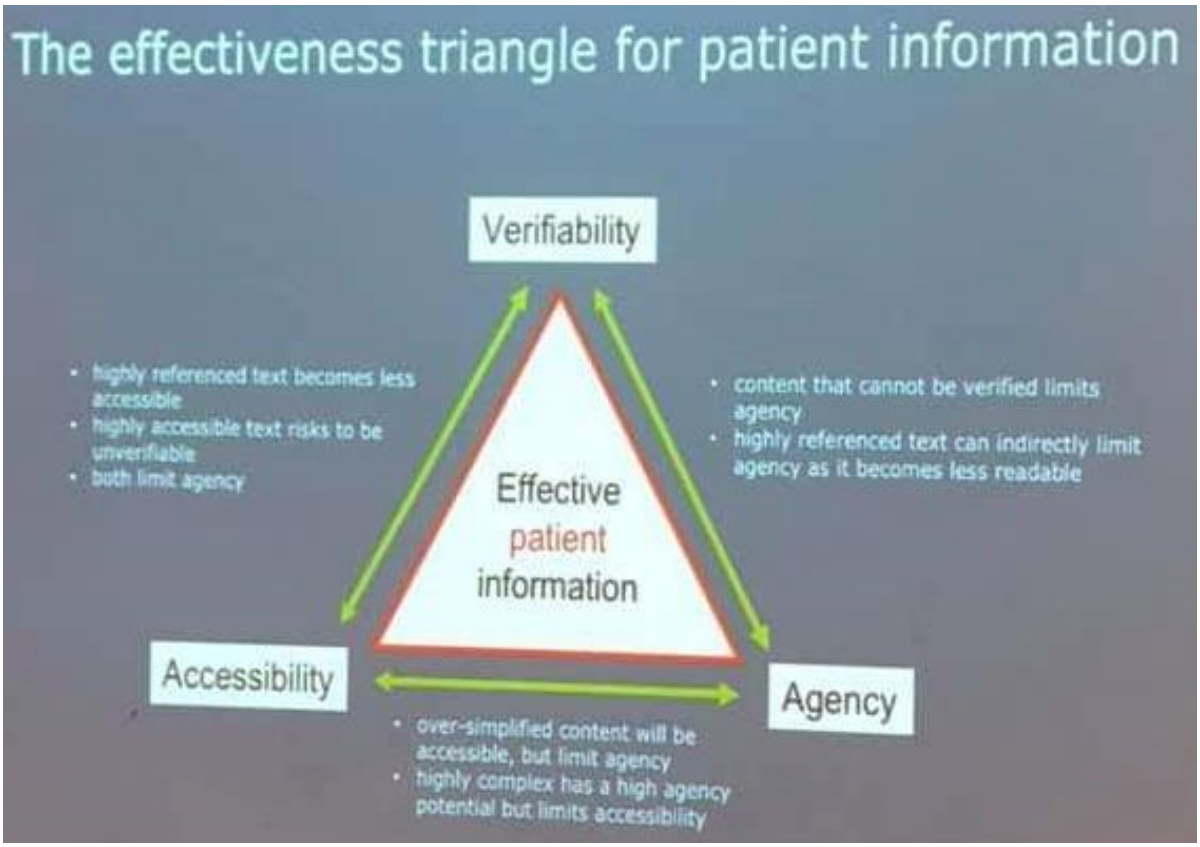
Four principles:

1. Patients first
2. No complaining -> solutions
3. Data, not opinions. Evidence based
4. Pro-active

Three pillars:

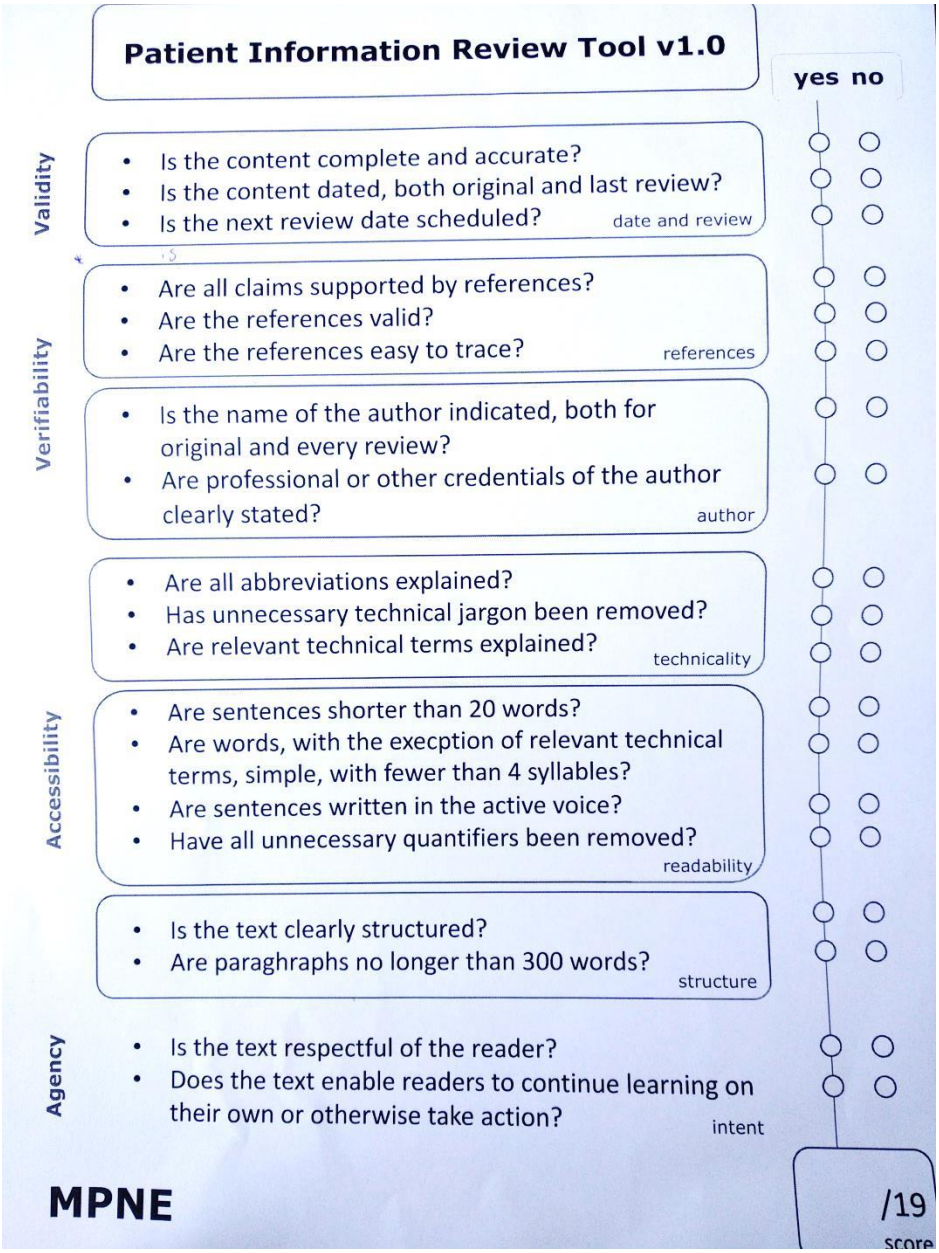
1. Know your disease
2. Systems
3. Tools, how to communicate (Slack), personal tools to give a presentation, dropbox

How to talk to your oncologist. Take notes. Adults learn differently than children. Children are more open to everything new, adults wants answers to their questions.

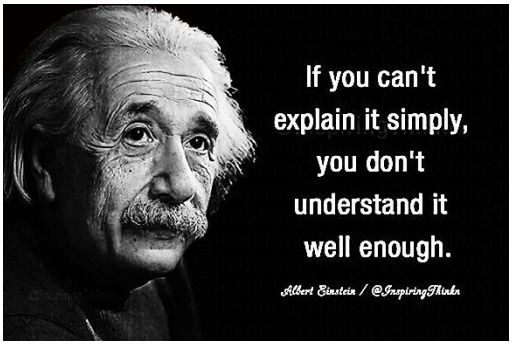



Agency is giving people empowerment.

Patient Information Tool 1.0




Abbreviations as little as possible, but some must (HTA, NRAS, BRAF, EMA)
Text like ‘has been observed’ is passive, get rid of it.
Don’t put patients in a lower position.



MPNE Quickstart: is for new comers.
MPNCEE for everyone
MPNNordics: Nordic countries
MPNERARE: ocular and pediatric melanoma
Krusenberg: hubsmeeting, for advocates

Projects in drugsafety: fair medicine, what can we do when working with pharma?

MPNE hubs: what's important? What do we need to be a good patient advocate? We came up with: (prioritize)

- Knowledge
    - Expertise
    - Recourses
- Human recourses
    - Capacity
    - Volunteers
    - Skills
    - Patients
- Money
- Structure
    - Kits
    - Tools
    - Structural

**Melanoma in a Nutshell**

Melanoma doesn't stay in one place (compare chair in airplane, fat person sitting ni the other chair). It pushes away other cells.

Metastases to brain (reason stem cell has same origin?)

Patient tested for BRAF: switch which cannot be turned off

1. Targeted therapy turns off switch: MEK inhibitor. Works for 50%, 50% mutant. BRAF mutation is not inhereditary. Red hair, freckles, etc. is
2. Check point inhibitors (nobel price), autoimmune system. Compare knife flying through kitchen. Blocker to break
3. Immune therapy - last option. Injection in tumor. Not available

**Know your stage**

1. Tumor
2. Lymphnodes
3. Metastasis

AJCC classification has changed

Stage 1+2 is skin
Stage 3 nearest lymph node
Stage 4 far from primary tumor

P – pathology report
T- tumor
NO- no metastases, no lymphnodes
M-LDH in blood

Example: pT3bN2bMO is stage 3b

**Imaging explained**, luc Vautmans

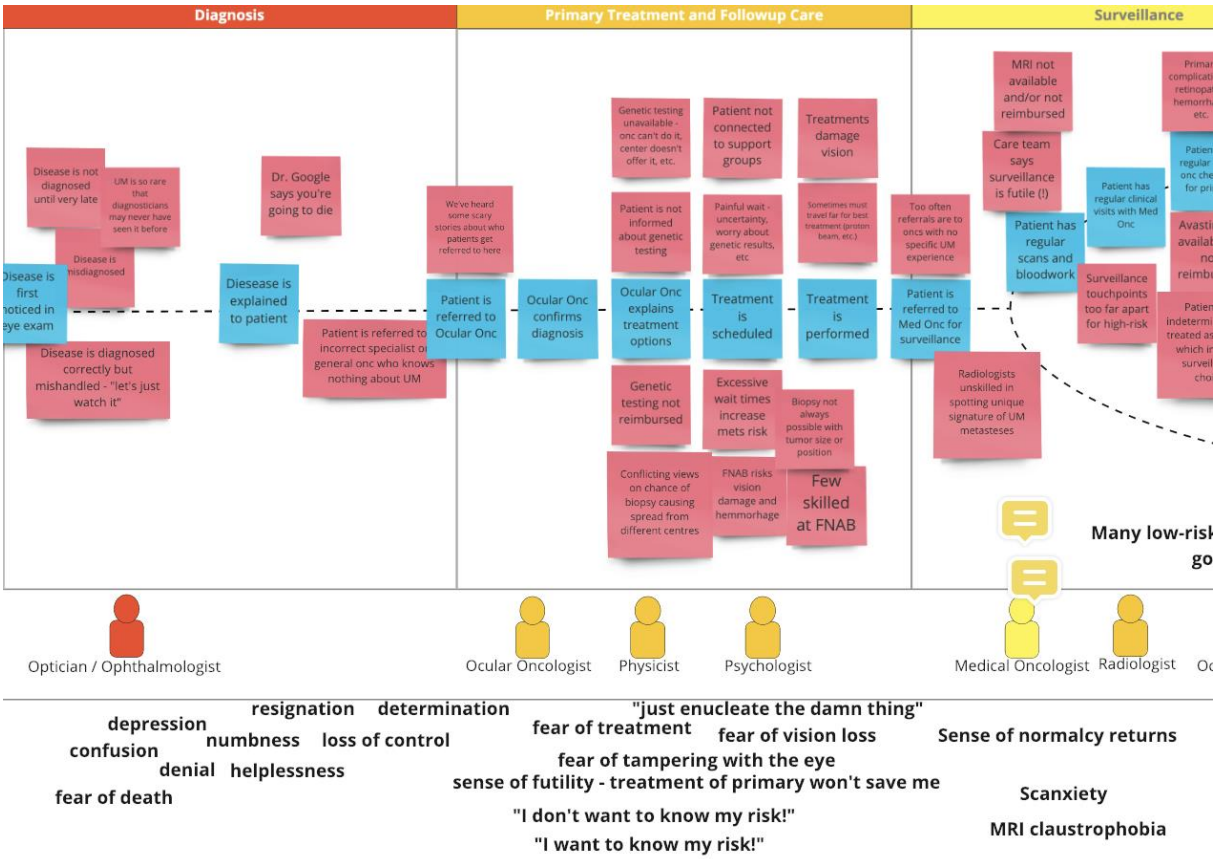
CT scan – high dose of radiation
PET scan – 'sugar', radioactive(fluorodexyglucose). Not good for brain (takes sugar too fast)
MRI scan – no radiation, expensive
CT + PET scan – very clear image, high dose of radiation

MPNE rare, Bettina

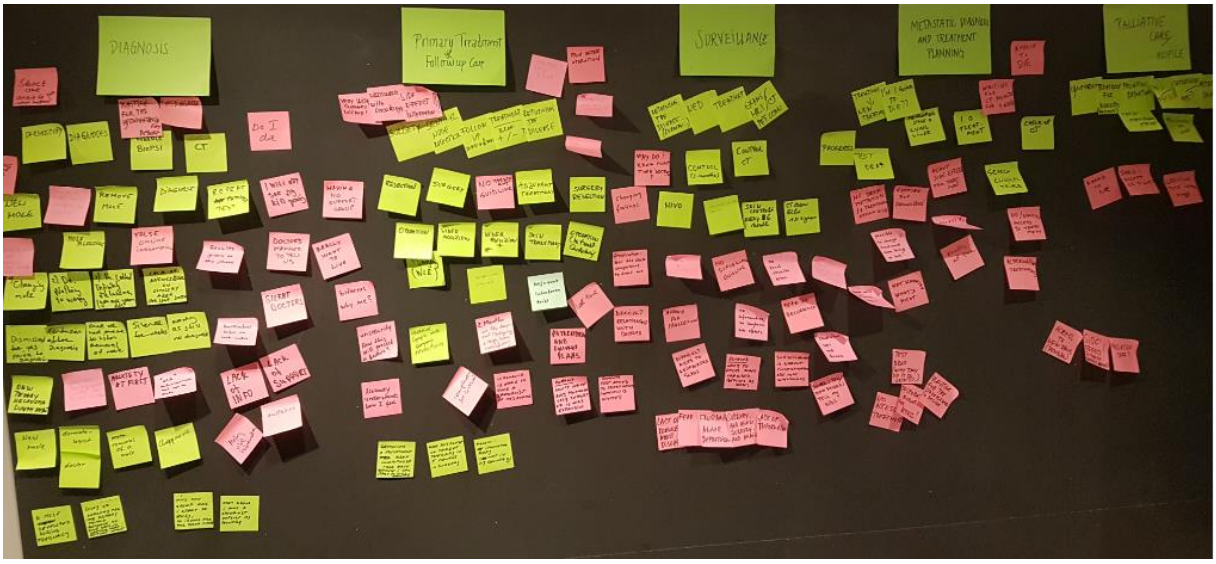
1. Research
    - Biobank
    - Registries
    - Genetic testing
    - Research to NRAS
2. Standards

    - Protocols
    - (international) guidelines
    - Registry to learn about risk
3. Medical community
    - Train to the docs
    - Do doctors have a clue?
    - 2nd opinion
    - ignorance
4. Patient pathways
    - Patient journey
    - Healthcare path
    - Is there a structure/approach to my disease?
    - Finding specialized centers
    - Expertise centers
    - Connecting experts
5. Access to new treatment
    - Treatments available, where to receive it?
    - Clinical trials and access
    - Compassionate use
    - Access to innovation
6. Early and correct diagnosis
    - Prevention
    - Diagnosis
    - Stage?
    - Late diagnosis
    - Miss diagnosis
7. Advocacy
    - Patient support
    - Overlapping interests
    - How to find co-patients
    - Connecting patients
    - Patient support
    - Finding right information
    - Access to information
    - What if it is rare… people still need help

**Patient journeys, Andrew Evans, Sanne Wiingreen**




Red post-it's, prioritize. Sometime easy to solve #1, sometimes hardest problem #1. Framework is to see where all the pain is. Stage of a patient journey can be split too. Which doctors involved? What went wrong? "pain in the ass". Mention is country related. Emotions – quotes.



**Infographics, Berit Eberhardt and Gilly Spurrier**

Google 'infographics canva' https://www.canva.com/create/infographics/

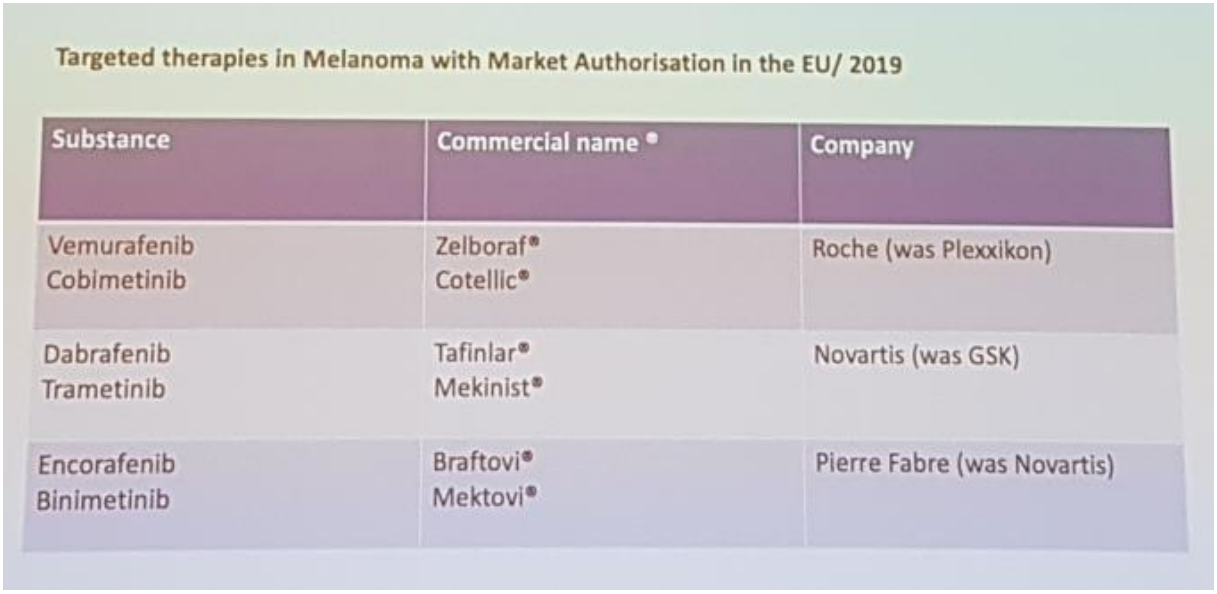
Side effects are filled in by doctors (CTCAE) ☹

Saturday

**Targeted therapies in melanoma, Bettina**

France first to start immunotherapy (not based on results).
Targeted therapy is for fast growing tumors
Adjuvant therapy stage 3+4 last options
Curative therapy is additional after surgery to heal.

Targeted therapy – combinations, different drugs, sometimes even stop => depending on oncologist. Inconsistent!



Targeted therapies in Melanoma with Market Authorisation in the EU/ 2019

| Substance | Commercial name ® | Company |
|---|---|---|
| Vemurafenib<br>Cobimetinib | Zelboraf®<br>Cotellic® | Roche (was Plexxikon) |
| Dabrafenib<br>Trametinib | Tafinlar®<br>Mekinist® | Novartis (was GSK) |
| Encorafenib<br>Binimetinib | Braftovi®<br>Mektovi® | Pierre Fabre (was Novartis) |

**Tumor heterogeneity as driver of resistance to targeted therapy, Julia Boshuizen**

Abstract article from Julia Boshuizen:

Intratumor heterogeneity is a key factor contributing to therapeutic failure and, hence, cancer lethality. Heterogeneous tumors show partial therapy responses, allowing for the emergence of drug-resistant clones that often express high levels of the receptor tyrosine kinase AXL. In melanoma, AXL-high cells are resistant to MAPK pathway inhibitors, whereas AXL-low cells are sensitive to these inhibitors, rationalizing a differential therapeutic approach. We developed an antibody-drug conjugate, AXL-107-MMAE, comprising a human AXL antibody linked to the microtubule-disrupting agent monomethyl auristatin E. We found that AXL-107-MMAE, as a single agent, displayed potent *in vivo* anti-tumor activity in patient-derived xenografts, including melanoma, lung, pancreas and cervical cancer. By eliminating distinct populations in heterogeneous melanoma cell pools, AXL-107-

MMAE and MAPK pathway inhibitors cooperatively inhibited tumor growth. Furthermore, by inducing AXL transcription, BRAF/MEK inhibitors potentiated the efficacy of AXL-107-MMAE. These findings provide proof of concept for the premise that rationalized combinatorial targeting of distinct populations in heterogeneous tumors may improve therapeutic effect, and merit clinical validation of AXL-107-MMAE in both treatment-naive and drug-resistant cancers in mono- or combination therapy.

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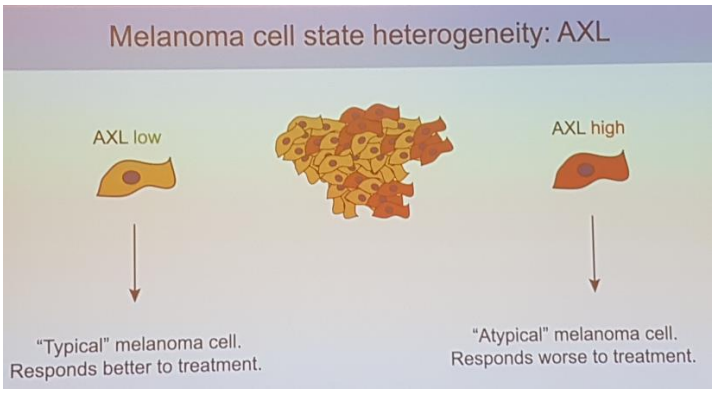
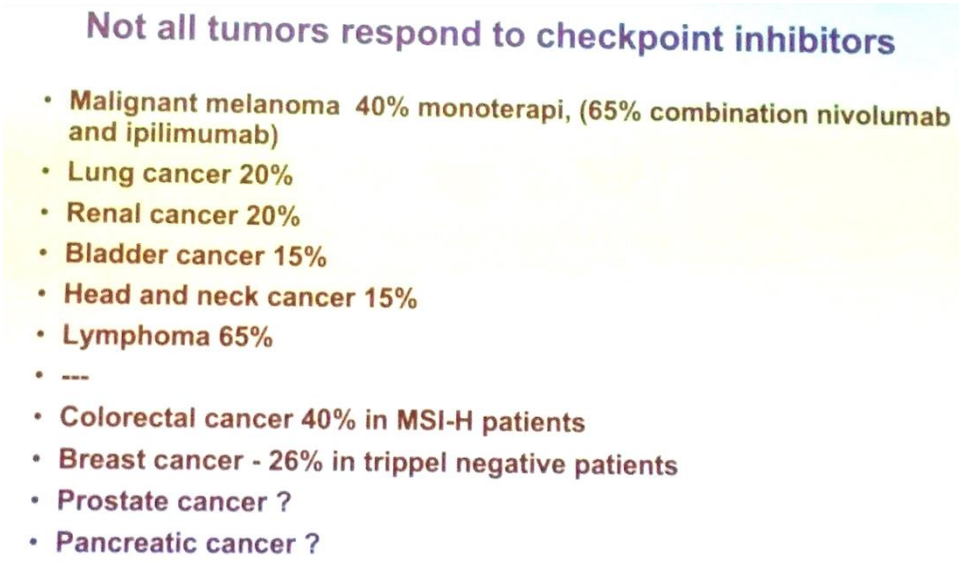
In a tumor cell there are often more mutations. Melanoma has the highest number of mutations in a tumor.
PTEN presence: responds better to immunotherapy. PTEN absent: resistant to immunotherapy.

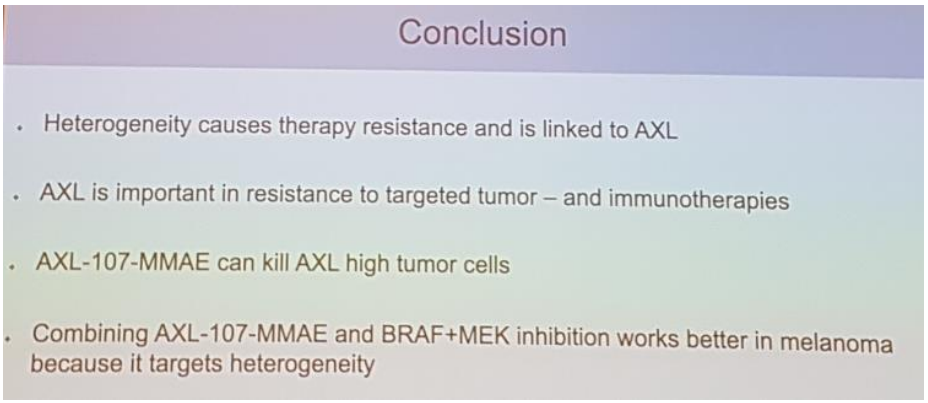



Anti body drug conjugates (ADC). Drug looks for AXL cells.
Resistant to therapy – acquired resistance to therapy.

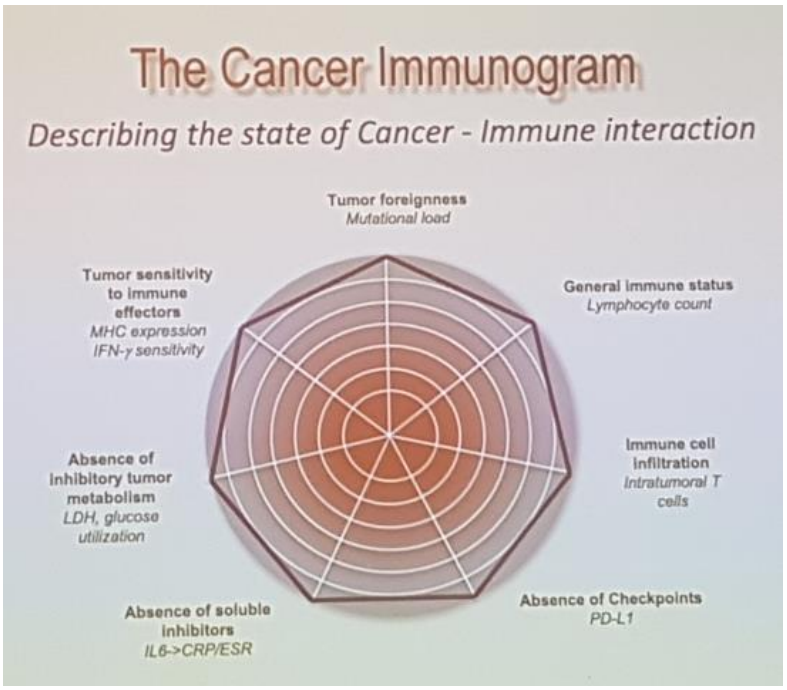
## Ways of Improving Immunotherapy

- Determine optimal dose of checkpoint inhibitors: 1mg/kg, 3mg/kg, 10mg/kg ; Q2 week, Q 3 week, 4 week, Q 3 month
- Treat the «right» patients
  - Biomarkers
- New combinations of checkpoint inhibitors
- Co-stimulation rather than inhibiting the inhibitors
- Treat in the adjuvant or neoadjuvant setting rather than in the metastastic ?
- Challenge resistance
- Break the «PD-1 ceiling» - combinations recruiting novel T- cells clones.
  - *TCR*
  - *Cancer vaccines*




**Resistance to immunotherapy: an overview, John Haanen**




The problem with vaccination: immunotherapy is started first, then they develop a personal vaccination and in a 2nd phase the vaccine is given to the patient. You get good results, but don't know if it's related to the immunotherapy or vaccine.

T cell vaccination