Chemotherapy Dose Banding

Development and Implementation

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Disclosure

Relevant Financial Relationship

- None

Off-label Investigational Uses

- None

Summary

- Learning Objectives
- Self Assessment Questions
- Drug dosing
- The Clinical perspective on Dose Banding
- Implementation by example

Learning Objectives

- Understand the benefits and evidence for dose rounding
- Practical implementation of chemotherapy and biological agents

Self-assessment questions

1. Does dose banding affect the patient's clinical response to treatment?

2. Does dose banding also apply to the anti PD-1 antibodies?

3. Can dose banding overcome chair time issues?

Drug Dosing

How did we get there?

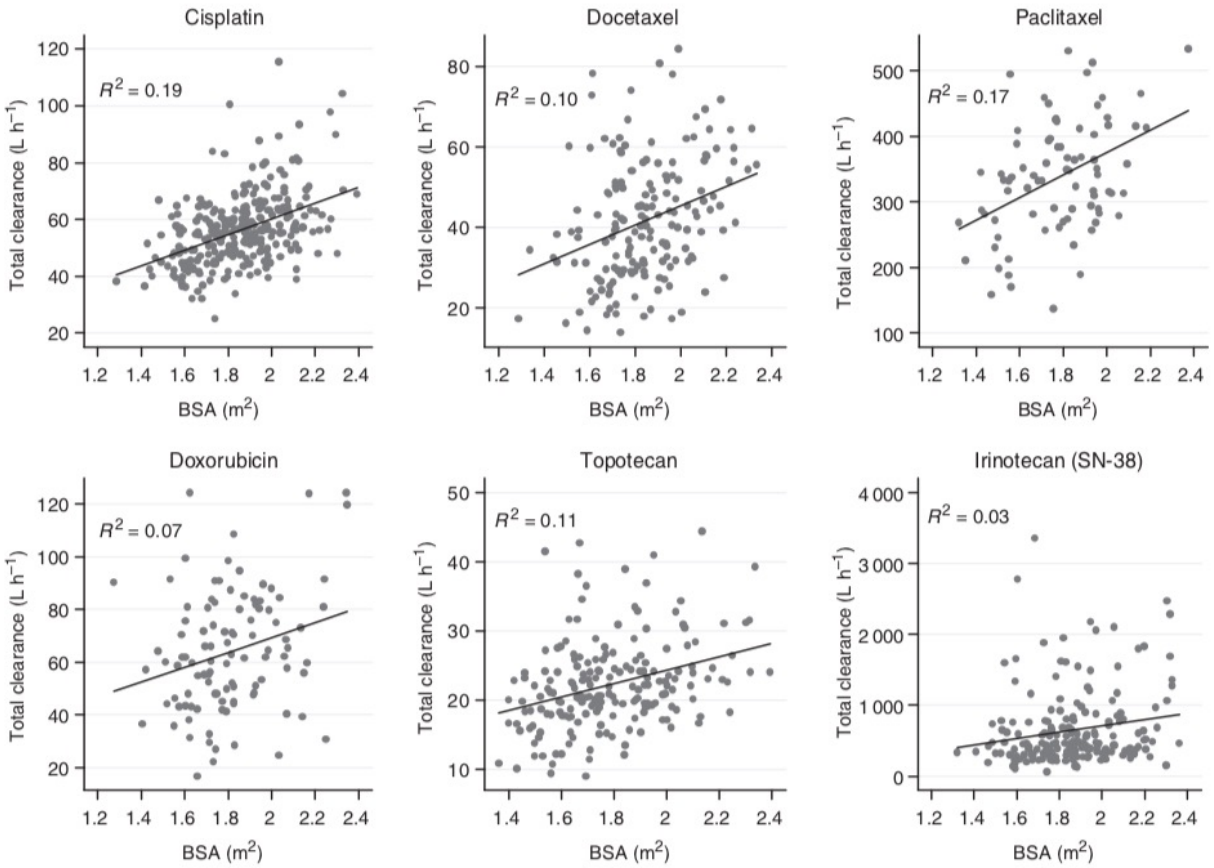
MTD

- Maximum tolerated dose = 1 dose less to the (toxic) dose that elicits DLT (Dose limiting toxicity)
  - Highest dose with accepted toxicity
- Determined bij Pharmacodynamics
- Detemined in Phase I study:
  - Bias in patient eligibility vs patients in real life
- No evidence on late / chronic use toxicity.
- Premise: that toxicity equals efficacy and vice versa?

BSA

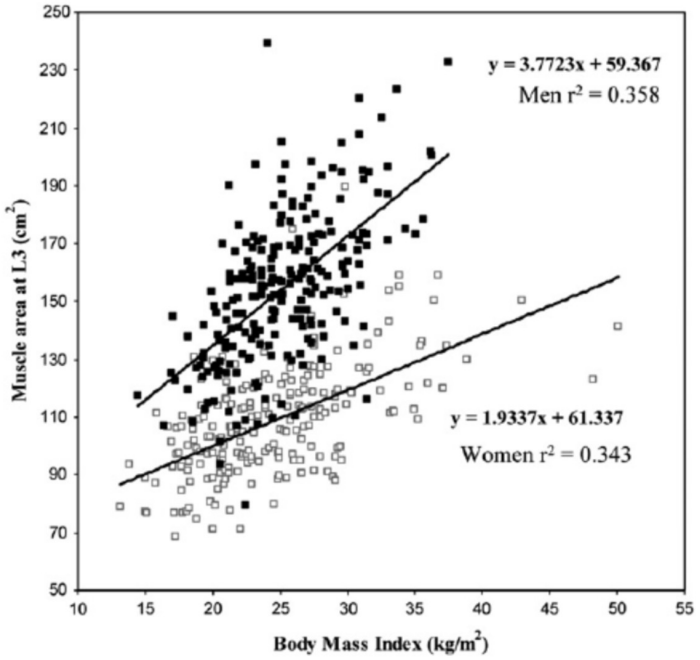
- Body Surface Area in use since 1958
- Faulty but useful:
- Measurement of volume (?) ⏚ elimination capacity
- However
  - Clearance / elimination is not correlated with BSA
  - No Correlation with AUC
  - Not/less useful in cachectic or sarcopenic patients
  - What about gut microbiotica?

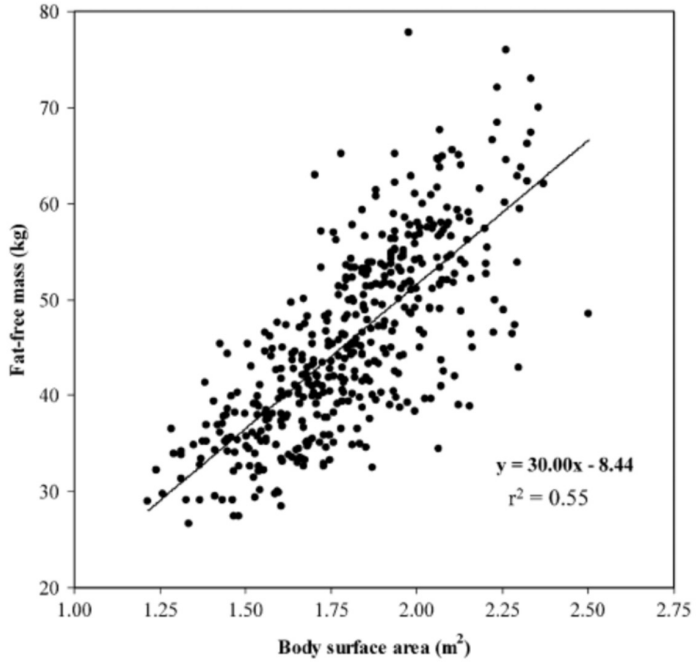
Problems with BSA: correlation with clearance



Chatelut E et al 2012, BJCancer: 107:1100-1106

Problems with BSA: Correlation with cachexia





Baracos V et al. 2010. Am J Clin Nutr 91: 1133S-1137S.

Dose banding does not solve the BSA conundrum

- It is a practical way to manage efficiently:
  - Reduce patient waiting time
  - Plan pharmacy production
  - Reduce the potential of medication errors
  - To allow Quality Control of preparations
  - Reduce drug wastage

Clinical perspective on Dose Banding

Of Systemic Anti-cancer Therapies

Clinical perspective on Dose banding

- Principles in treatment:
  - Do no Harm
  - Efficacy: in treating a patient (not the disease)
  - Toxicity: both short an long term
  - QoL (Quality of Life)

Clinical perspective : dose rounding: Hematology / Oncology Pharmacy Association (HOPA)

- Dose rounding for biologicals
  - 10 %
  - Nearest vial size
  - (egrituximab, bevacizumab, trastuzumab, cetuximab, ipilimumab, and gemtuzumab)
  - Recommendation is based on AUC variations (however development of therapy can be discussed as well: frequency – dosing according to MTD etc.)
- Dose rounding for antibodies with cytotoxic constituents
  - Dose rounding for cytotoxics : 5%
- Same dose rounding rules in palliative care as in curative therapy

Fahrenbruch R et al, Journal of Oncology Practice 2018 14:3, e130-e136

Clinical perspective : dose rounding: Hematology / Oncology Pharmacy Association (HOPA)

- “Classic” chemotherapy: dose rounding within 5% to 10%, accepted. Premise = no negative impact on safety or effectiveness of the therapy. Standard dose adjustments to improve patient tolerance and response are generally in the range of 20% to 30%,
- Most oral anticancer agents:
  - flat based dosing
  - Minority are prescribed using BSA
  - Rounding to nearest capsule/tablet
  - Often lack of good biomarker – fasting dose -

Fahrenbruch R et al, Journal of Oncology Practice 2018 14:3, e130-e136

Clinical perspective: exercice is pragmatism

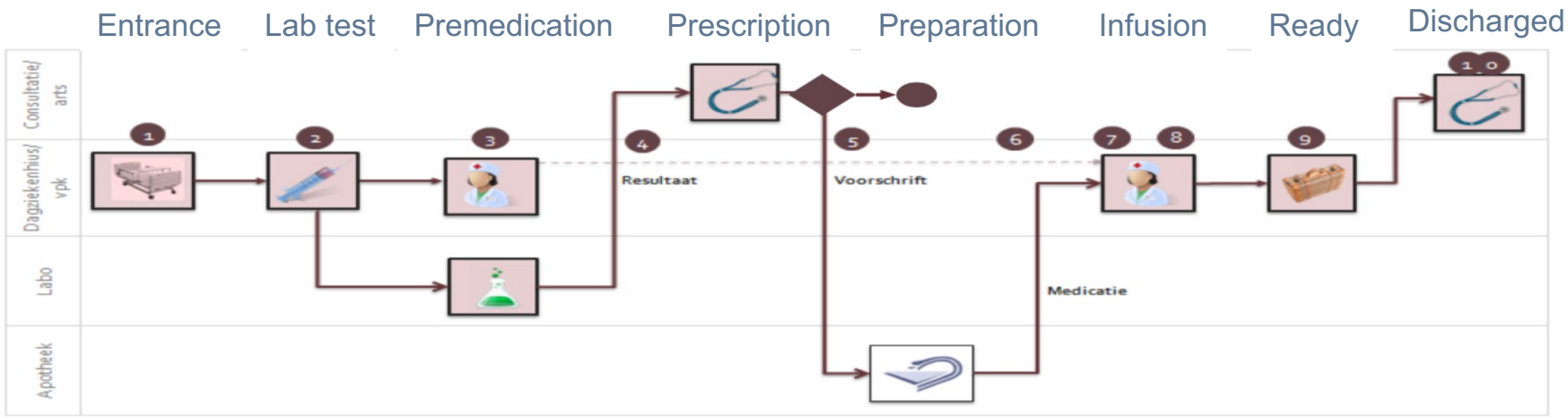
- Administration of any anti-cancer drug:
  - Certified Quality of preparation
  - Reproducible in large numbers
  - Safe distribution / handling / administration
  - Timely “ CHAIR TIME”

  - Controlled:
    - Uniform registration of side effects (NCI PRO CTC-AE)
    - By the use of patient reported outcomes
    - By the use of validated Qol – Questionnaires
    - continuously or intermittently

Example of Implementation

Of Systemic Anti-cancer Therapies

Evaluation of the turn around time including ”Chair time”



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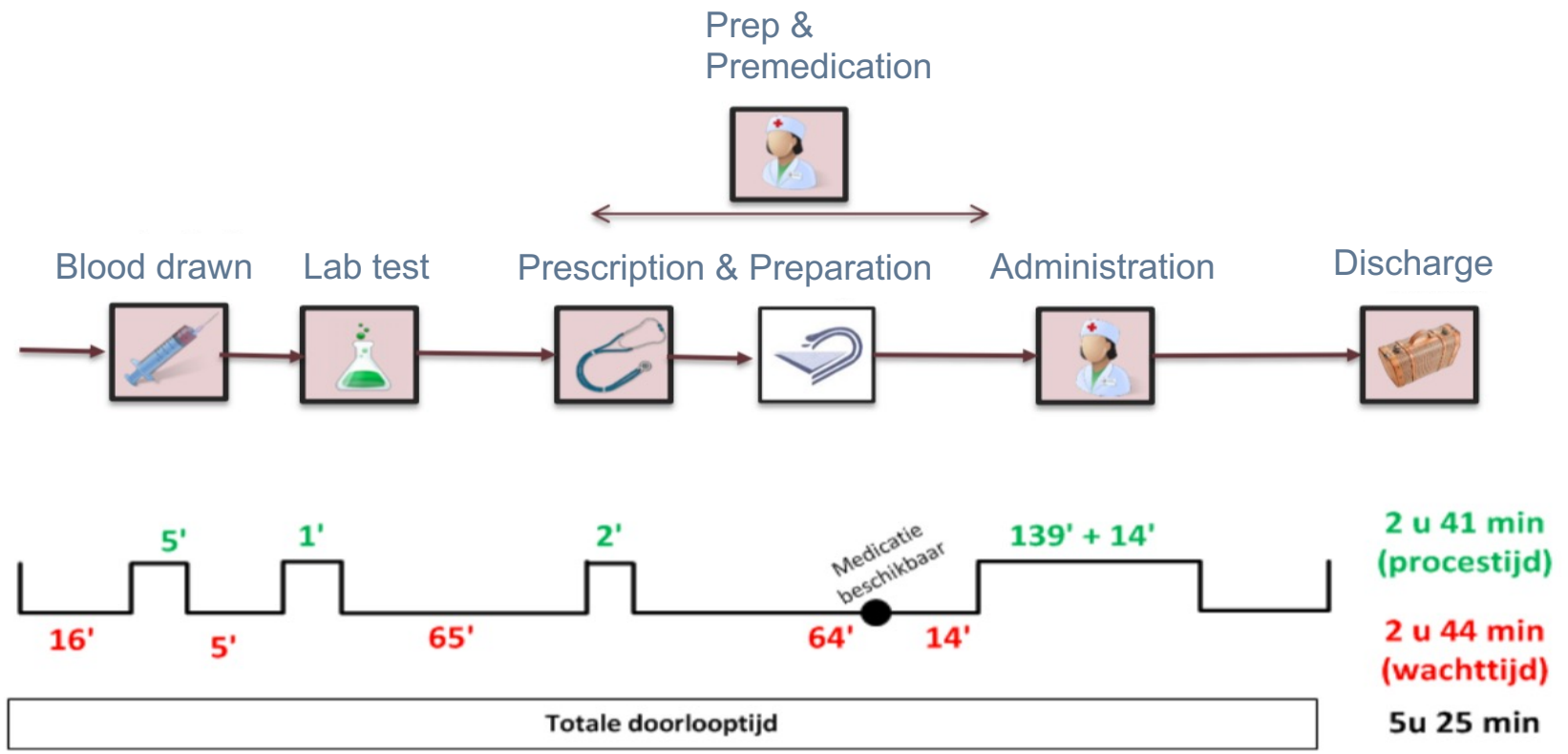
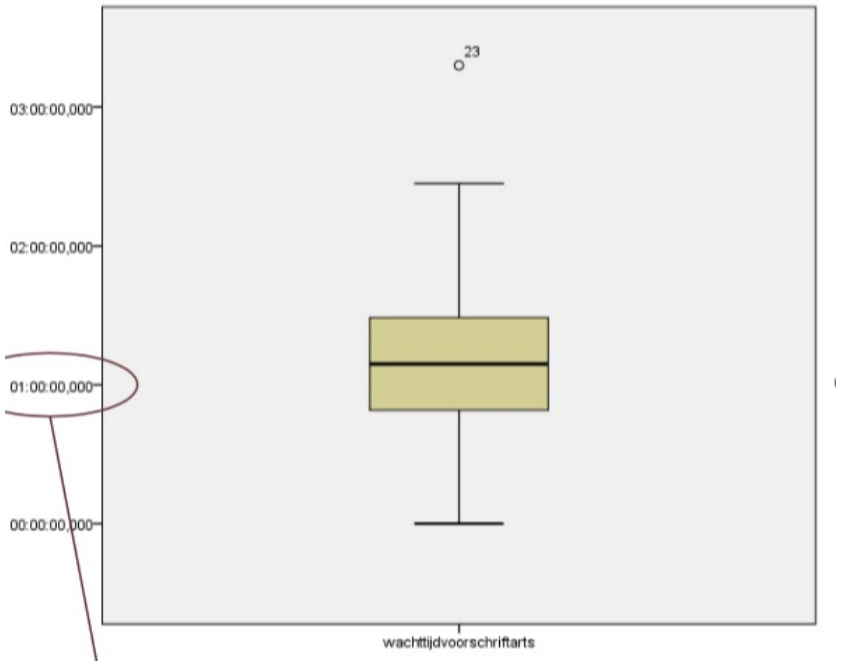
Measuring is knowing

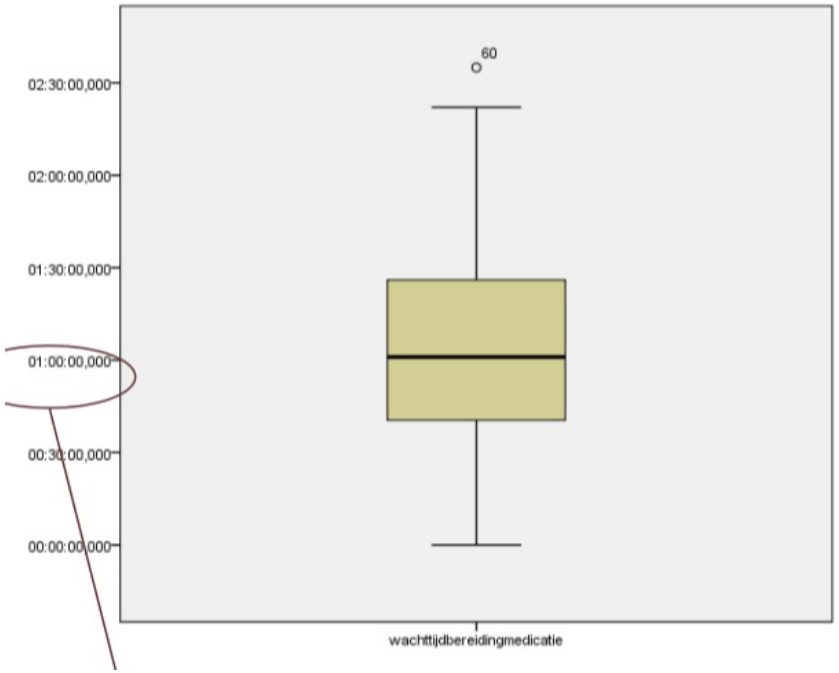


2 Major problems:

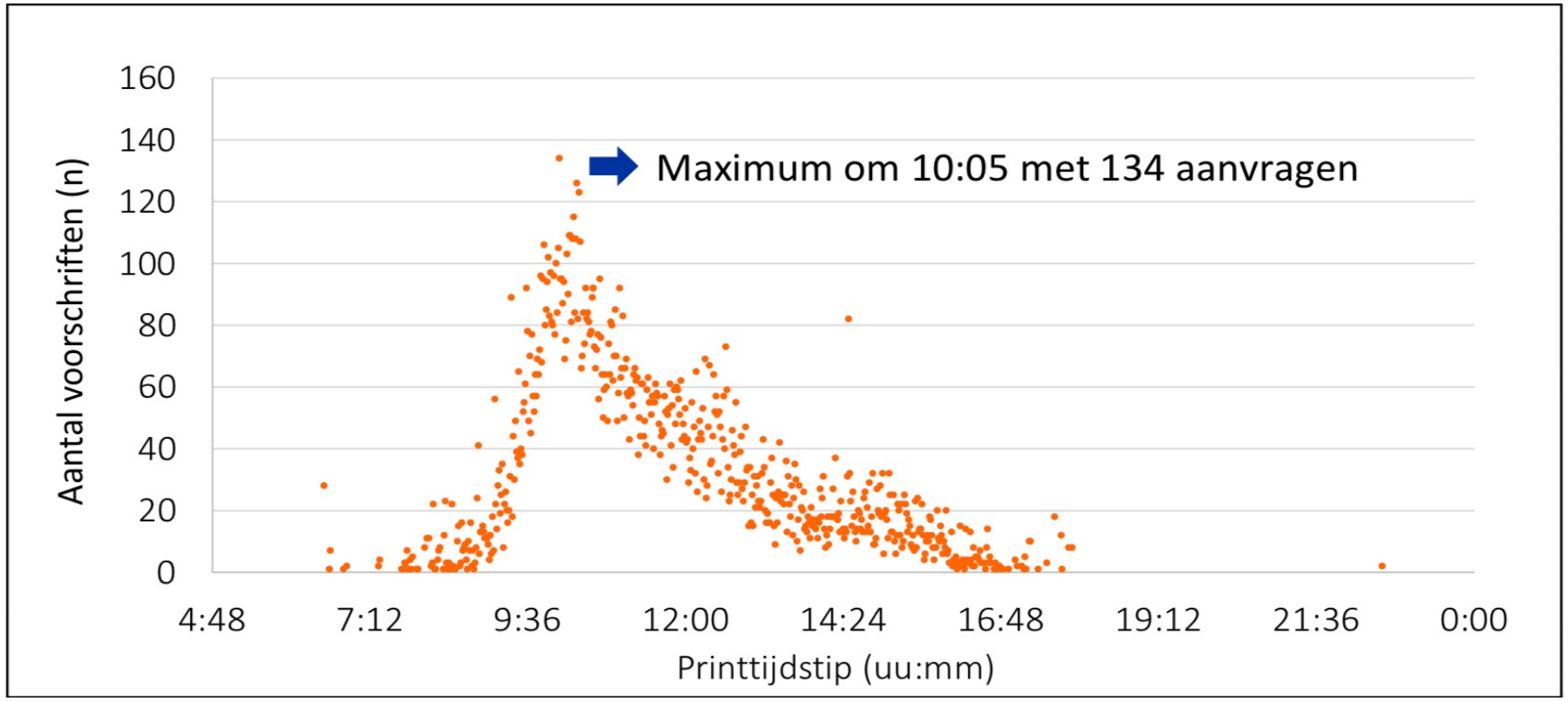
- Waiting for physician



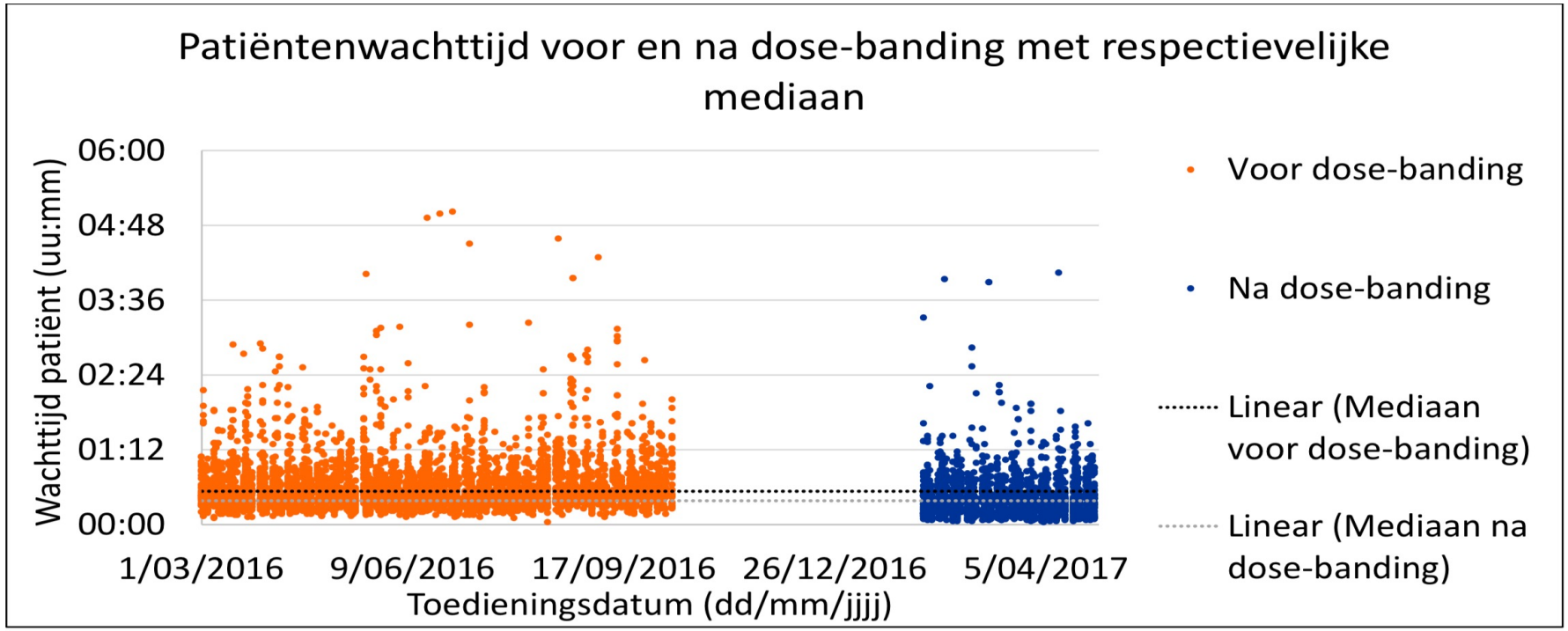
- Waiting for preparation



Density of prescription at 10:05u



Total waiting time after dose banding



Median before / after dose banding 00:32 / 00:23 (p<0,001)

Take Home Messages

1. This will become the era of molecular medicine, immune – oncology and farmacogenomics.
2. BSA is a practical tool that does not reflect real intervariable pharmacodynamics.
3. Dose Banding is able to overcome Chair time issues
   - and to support transmural Cancer care (hospital at home initiatives).


Thank you
for your attention
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