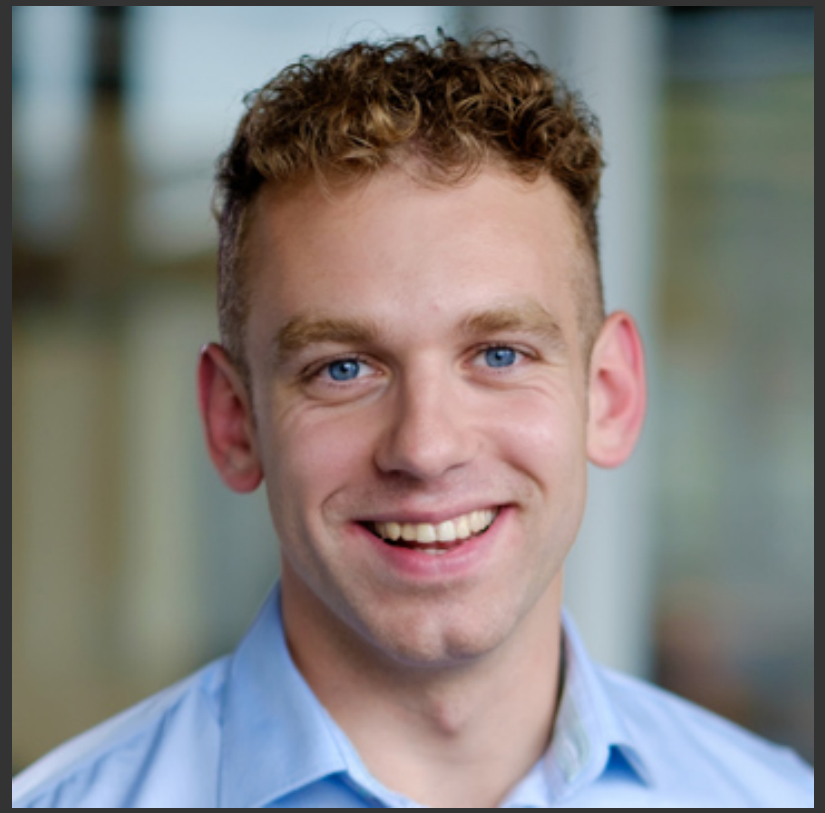
RWD and EA

Presentation for RSNN-EMA Workshop
17NOV2020



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Research consortium

Public-Private Collaboration (PPS)

ErasmusMC

Department of Biostatistics/HTA

myTomorrows

RWD Department

Health~Holland

Topsector Life & Health

Expanded Access

Non-trial (pre-approval) access to unapproved medicine.

For patients who:

- Cannot be treated with approved medicine
- Cannot participate in clinical trials
- Seriously debilitating or life-threatening condition
- May benefit from investigational therapy (risk/benefit)

Real-World Data

Data collected outside of conventional (controlled) trials.

- PASS/PAES
- Electronic Health Records
- Claims and billing activities
- Product and disease registries
- Patient-reported outcomes
- Social media
- Expanded Access

original article

Annals of Oncology 19: 1320–1326, 2008
doi:10.1093/annonc/mdn050
Published online 15 March 2008

Report of an international expanded access program of imatinib in adults with Philadelphia chromosome positive leukemias

R. Capdeville[1]*, T. Krahnke[1], A. Hatfield[1], J. M. Ford[1], I. Van Hoomissen[2] & I. Gathmann[1]

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Received 18 November 2007; revised 30 January 2008; accepted 1 February 2008

Original Study

Analysis of Efficacy and Prognostic Factors of Lenalidomide Treatment as Part of a Dutch Compassionate Use Program

Evelien Kneppers,[1] Henk M. Lokhorst,[1] Corien M. Eeltink,[2] Gerwin Huls,[3] Marie José Kersten,[4] Jan Koedam,[5] Monique C. Minnema,[1] Marinus H. J. van Oers,[4] Reinier A. P. Raymakers,[6] Martijn R. Schaafsma,[7] Edo Vellenga,[3] Pierre W. Wijermans,[8] Shulamiet Wittebol,[9] Pieter Sonneveld,[10] Sonja Zweegman[2]

Real-world experience with cabazitaxel in patients with metastatic castration-resistant prostate cancer: a final, pooled analysis of the compassionate use programme and early access programme

Zafar Malik [1], Axel Heidenreich [1, 2], Sergio Bracarda [3], Alexandros Ardavanis [4], Philip Parente [5], Hans-Joerg Scholz [6], Ayse Ozatilgan [7], Evelyne Ecstein-Fraisse [8], Simon Hitier [9], Giuseppe Di Lorenzo [10]

ORIGINAL ARTICLE

DOI: 10.1016/j.arbr.2018.05.020

Compassionate Use of Lumacaftor/Ivacaftor in Cystic Fibrosis: Spanish Experience

Uso compasivo de lumacaftor/ivacaftor en fibrosis quística: experiencia española

Breast Cancer Res Treat (2007) 106:105–112
DOI 10.1007/s10549-006-9482-7

CLINICAL TRIAL

Fulvestrant ('Faslodex') in heavily pretreated postmenopausal patients with advanced breast cancer: single centre clinical experience from the compassionate use programme

Brigitte Mlineritsch · Oskar Psenak · Peter Mayer · Martin Moik · Konrad Namberger · Cornelia Hauser-Kronberger · Richard Greil

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Compassionate Use of Remdesivir for Patients with Severe Covid-19

Research question

- **What role does expanded access play in regulatory decision making?**

  To **identify**, **characterize**, and **compare** all FDA and EMA approvals that relied on real-world data from expanded access programs for **clinical efficacy** profile.

Received: 19 October 2019 | Revised: 19 December 2019 | Accepted: 6 March 2020
DOI: 10.1111/bcp.14284

ORIGINAL ARTICLE

Expanded Access as a source of real-world data: An overview of FDA and EMA approvals

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Funding information
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Aims: To identify, characterize and compare all Food and Drug Administration (FDA) and European Medicines Agency (EMA) approvals that included real-world data on efficacy from expanded access (EA) programmes.

Methods: Cross-sectional study of FDA (1955–2018) and EMA (1995–2018) regulatory approval documentation. We automated searching for terms related to EA in 22,506 documents using machine learning techniques. We included all approvals where EA terms appeared in the regulatory documentation. Our main outcome was the inclusion of EA data as evidence of clinical efficacy. Characterization was based on approval date, disease area, orphan designation and whether the evidence was supportive or pivotal.

Results: EA terms appeared in 693 out of 22,506 (3.1%) documents, which referenced 187 approvals. For 39 approvals, data from EA programmes were used to inform on clinical efficacy. The yearly number of approvals with EA data increased from 1.25 for 1993–2013 to 4.6 from 2014–2018. In 13 cases, these programmes formed the main evidence for approval. Of these, patients in EA programmes formed over half (median 71%, interquartile range: 34–100) of the total patient population available for efficacy evaluation. Almost all (12/13) approvals were granted orphan designation. In 8/13, there were differences between regulators in approval status and valuation of evidence. Strikingly, 4 treatments were granted approval based solely on efficacy from EA.

Conclusion: Sponsors and regulators increasingly include real-world data from EA programmes in the efficacy profile of a treatment. The indications of the approved treatments are characterized by orphan designation and high unmet medical need.

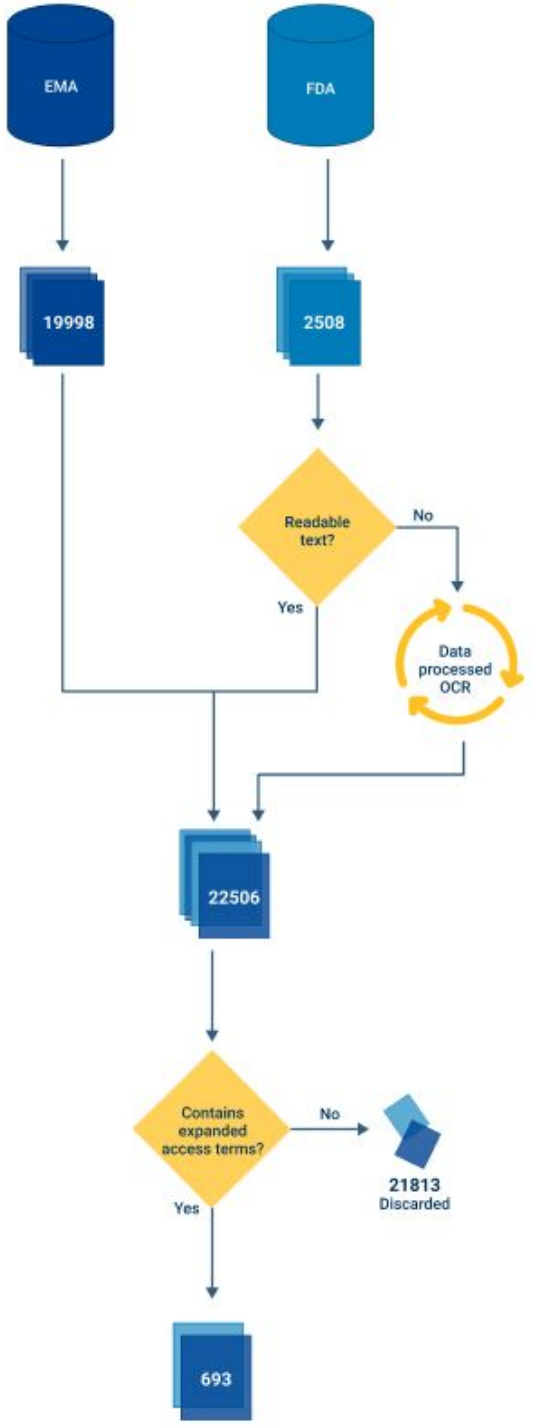
KEYWORDS
drug regulation, effectiveness, evidence-based medicine, health policy

Methods

Algorithmic approach.

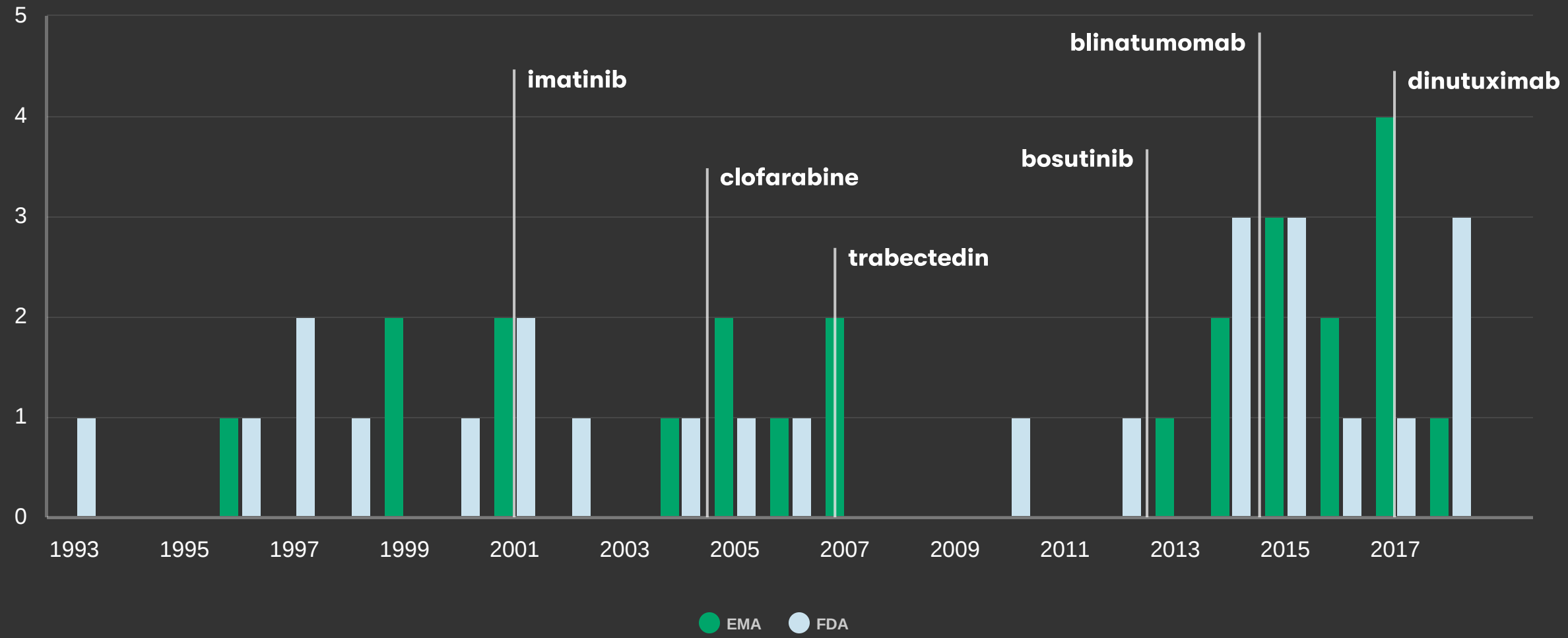
1. **Download FDA and EMA approval documentation**
2. **Process imagines to obtain text**
3. **Search text for expanded access terms**

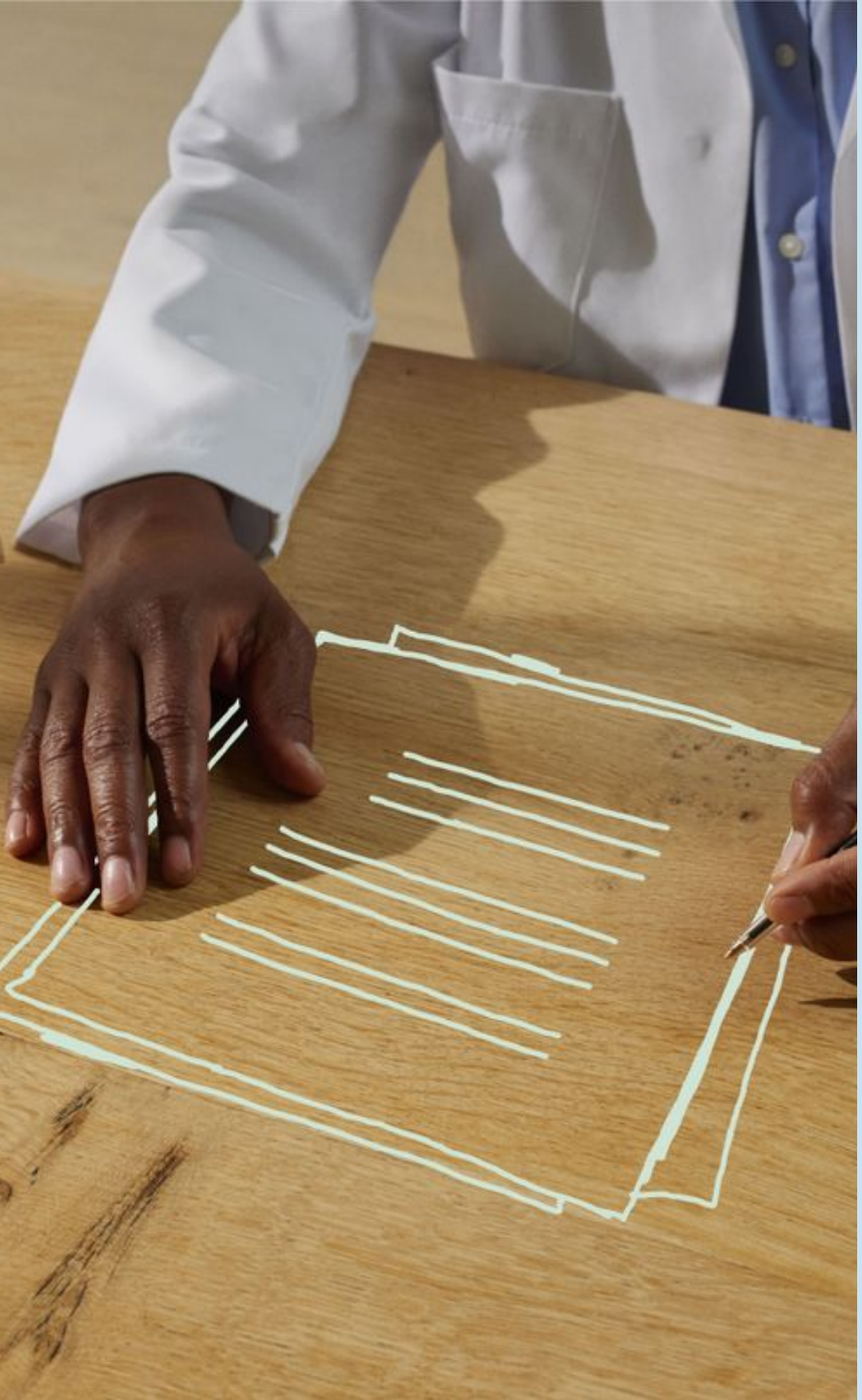
   ('compassionate use, special access, managed access...')
4. **Assess candidate documents for context of EA**
5. **Evaluate impact of expanded access for efficacy**



Timeline of EA RWD approvals

Supported by RWD from EA to support clinical efficacy





Regulatory framework

Who regulates Expanded Access?

1. **Responsibilities lie with individual Member States**
   - Countries allow data collection (FR) or **do not** (BE)

2. **EMA's Compassionate Use procedure**
   - CHMP offers **scientific opinion** on group programs

Contrasting statements

From the FAGG-AFMPS regulations (Belgium):

'The main goal of an UMN program is to provide an early access to a new innovative medicinal (...). Hence no other data except pharmacovigilance data can be gathered (...).'

Clinical Trial > Eur J Cancer. 2016 Jun;60:117-24. doi: 10.1016/j.ejca.2016.03.010. Epub 2016 Apr 20.

Results of the Belgian expanded access program of eribulin in the treatment of metastatic breast cancer closely mirror those of the pivotal phase III trial

Philippe Aftimos [1], Laura Polastro [2], Lieveke Ameye [3], Christiane Jungels [2], Jalal Vakili [2], Marianne Paesmans [3], Joanne van den Eerenbeemt [2], Alfino Buttice [2], Andrea Gombos [2], Dominique de Valeriola [2], Thierry Gil [2], Martine Piccart-Gebhart [2], Ahmad Awada [2]

Affiliations + expand

PMID: 27107326 DOI: 10.1016/j.ejca.2016.03.010

EMA on data collection

From the 'Guideline on Compassionate Use of Medicinal Products'

“The EMA does not allow efficacy data collection”- SE, BE

“Although safety data may be collected during compassionate use programmes, such programmes cannot replace clinical trials for investigational purposes.”

Final thoughts

Expanded Access programs generate RWE

EA has been a source of RWD since the 1990's and are being used more by EMA/FDA and pharmaceutical companies.

European harmonization

Member States and the EMA harbor unclear or confusing statements on the use of RWD from EA.

Treatment versus research

EA programmes primarily intended as a treatment pathway, but may secondarily be used to generate RWE. Conventional lines between **treatment** and **research** are becoming blurred.

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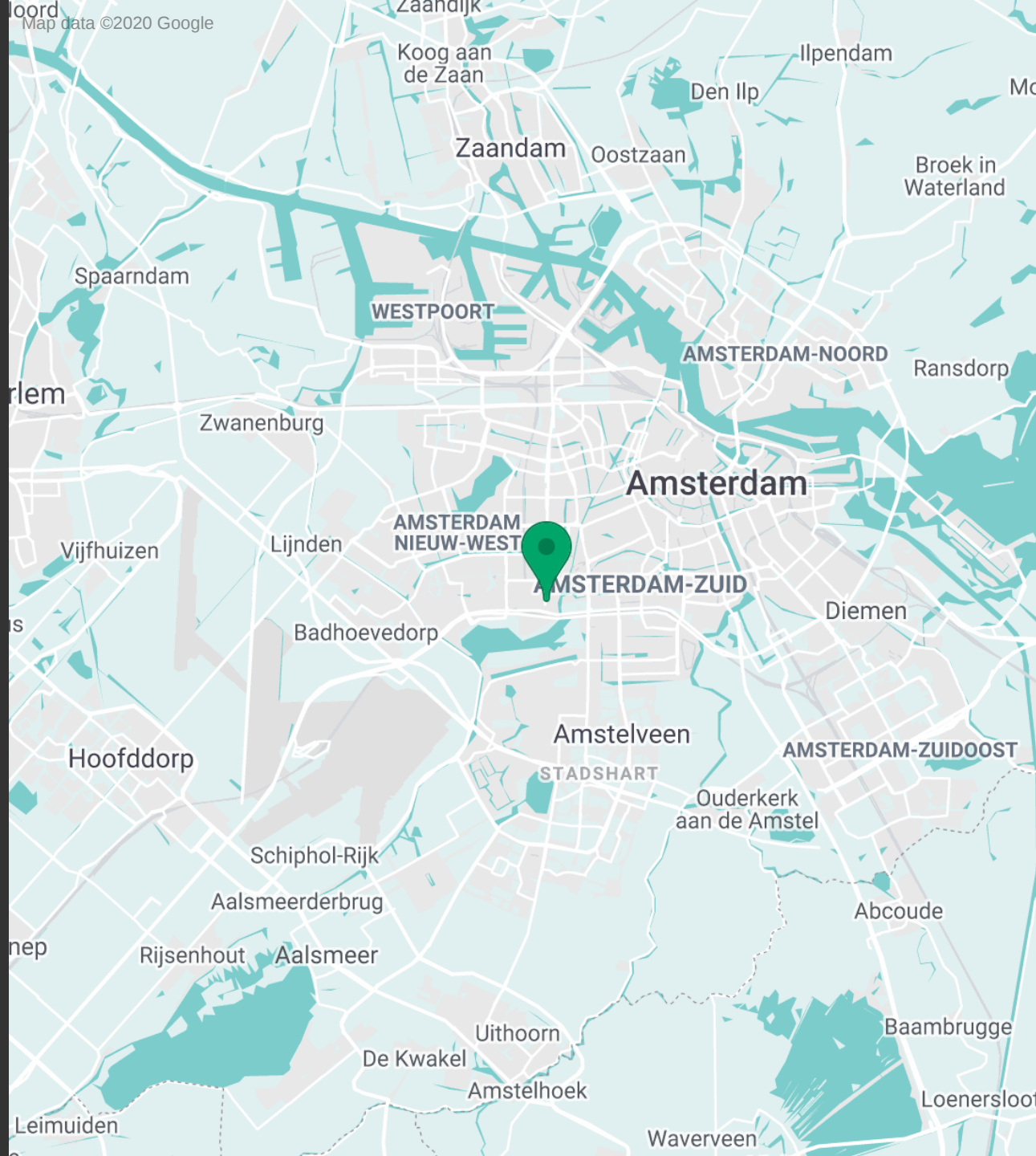

Thank you

Questions?