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Conditional marketing authorisation

Report on ten years of experience at the EMA

Presented by Zigmars Sebris on 27 June 2017
Regulatory Affairs Office, Human Medicines Evaluation Division

An agency of the European Union





Background

- Conditional marketing authorisation (CMA) **introduced in 2006**
- CHMP **Guideline** updated in 2016
- In response to public consultation comments it was suggested to publish a **report** on 10 years of experience with CMA
- Continuous **high interest** in the topic (internally and externally)
- Link with **other activities** on early access



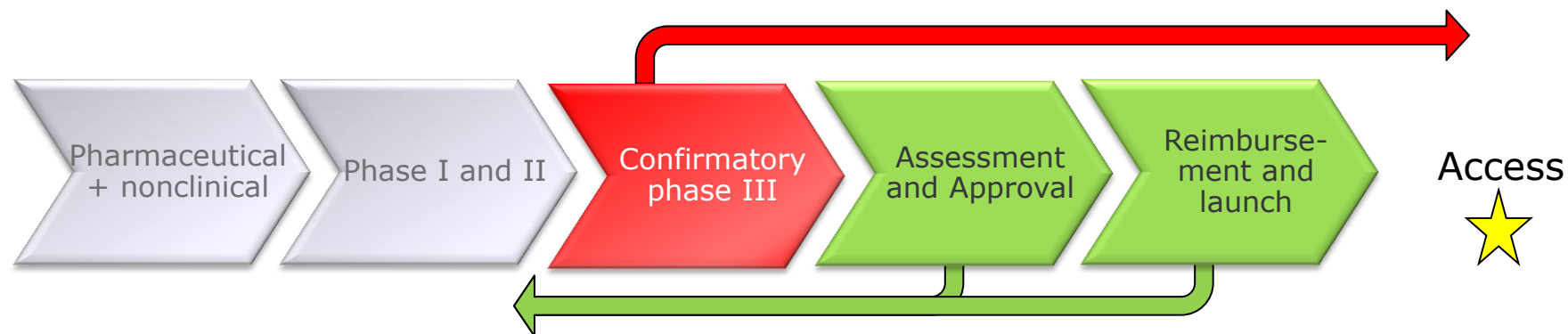
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at the European Medicines Agency

Conditional marketing authorisation

Authorisation before comprehensive data are available in order to address unmet medical needs, when benefits of early access outweigh the risks due to limited data



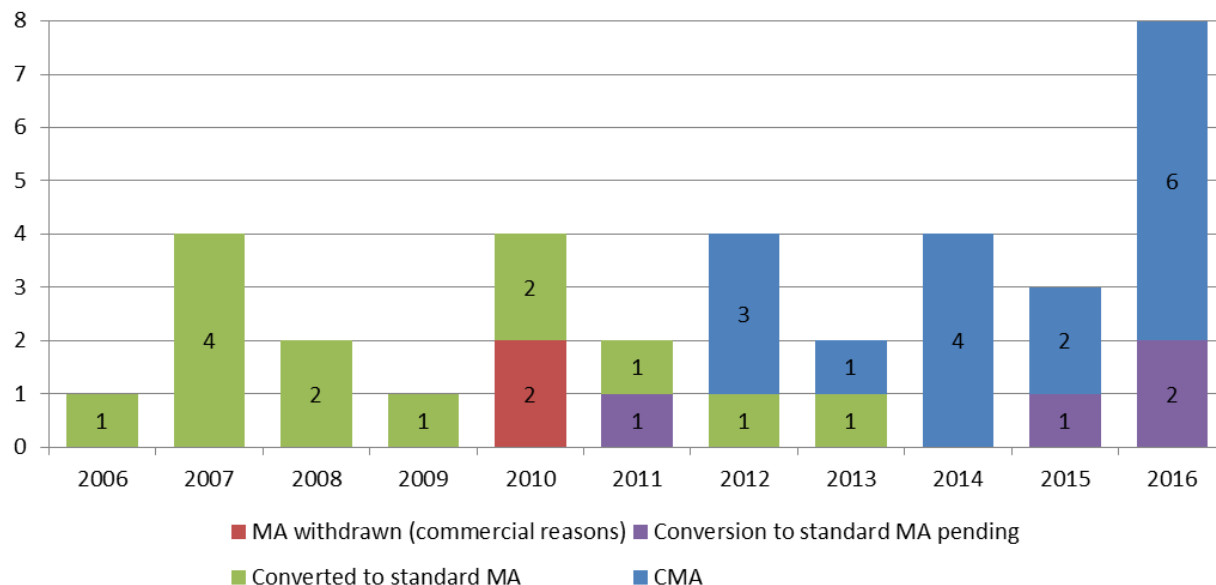
Main features:

- Product can be authorised several years earlier
- Comprehensive data are still generated after authorisation



Conditional Marketing Authorisations

CMAs granted 2006 - 2016 and their current status (N=35)

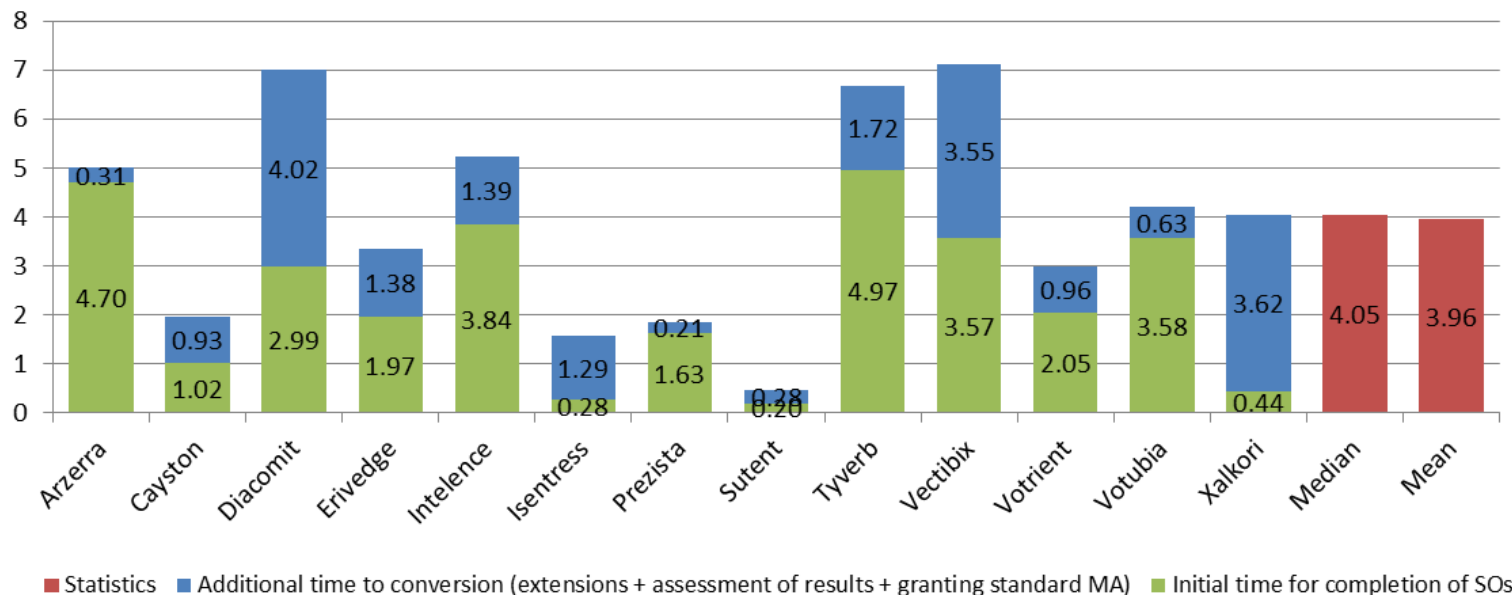


Apart from 2016, there is no clear trend in number of CMAs, which remain an 'exceptional' authorisation route



Conversion to standard MA

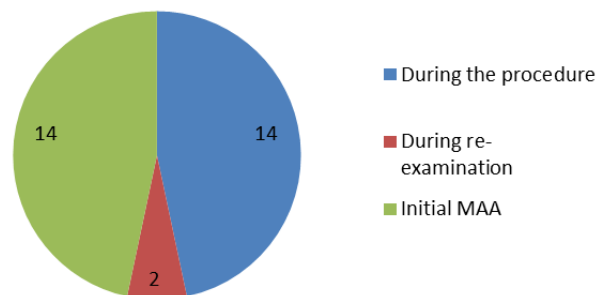
Time from granting CMA to conversion to full MA, all CMAs converted (N=13)



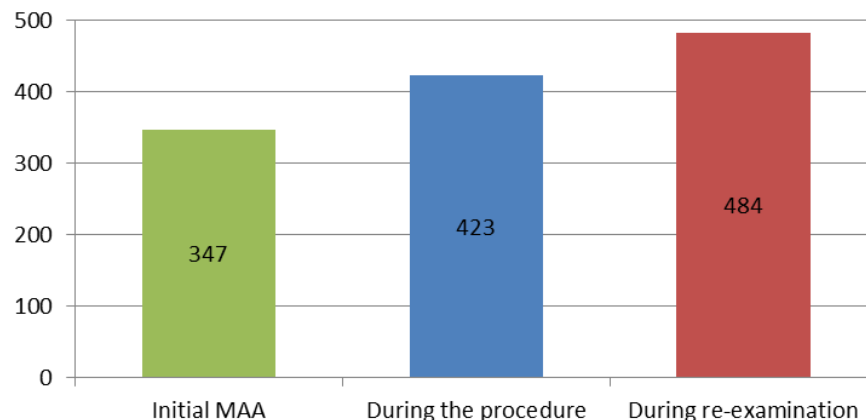
On average **within 4 years** a conditional MA is converted into a standard MA

Granting CMAs

Stage of procedure, when CMA was first considered, all CMAs (N=30)

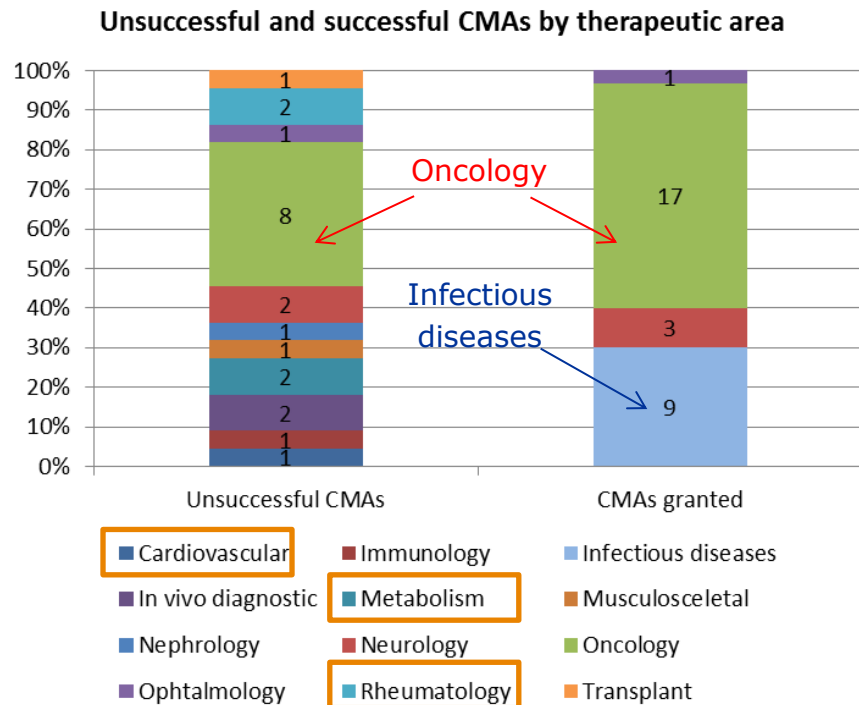


Mean duration of assessment (including clock-stops) by stage of first consideration of CMA (N=30)



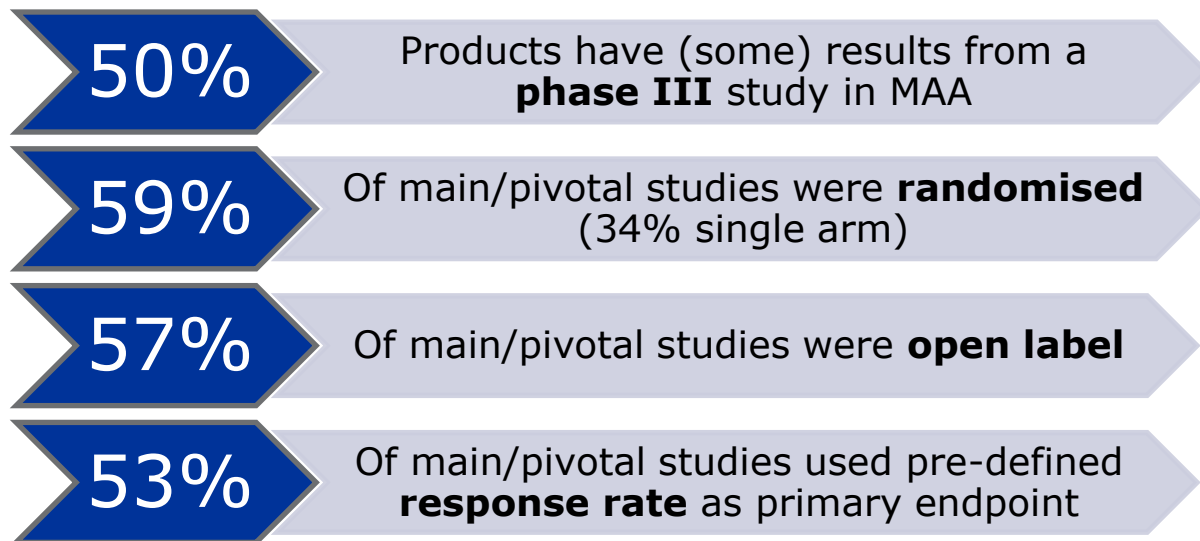
Reluctance in pro-active use of CMAs by industry – room for improvement in prospective planning.
CHMP has used the tool actively.
Only two CMAs granted following an accelerated assessment.

Comparison of successful and unsuccessful CMAs





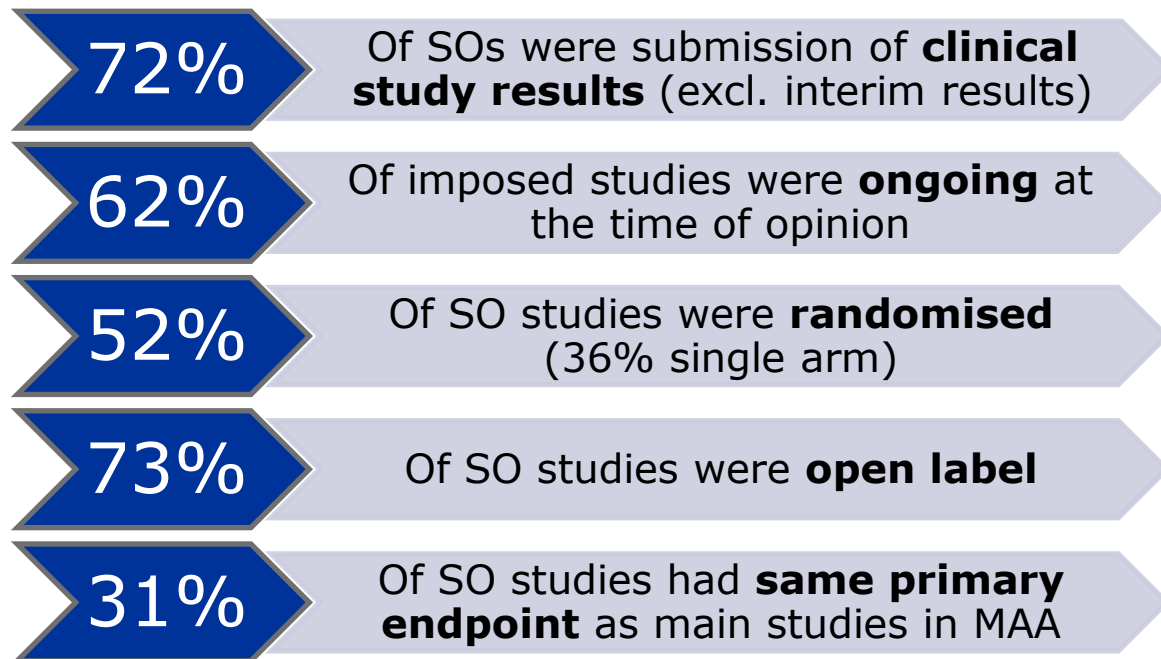
Data at the time of authorisation



“Typical” CMA as pivotal evidence has 2 phase II or III studies, most often open label, randomised and measuring a pre-defined response rate



Specific obligations (SOs) imposed

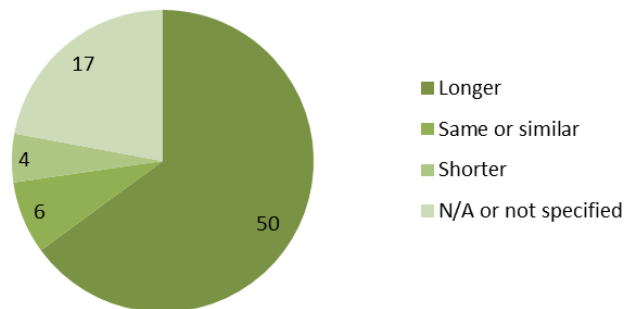


“Typical” CMA SOs required to conduct two phase II, III or IV efficacy and safety studies, which were open label, randomised or single arm, and measuring an endpoint often different from pivotal studies in CMA application



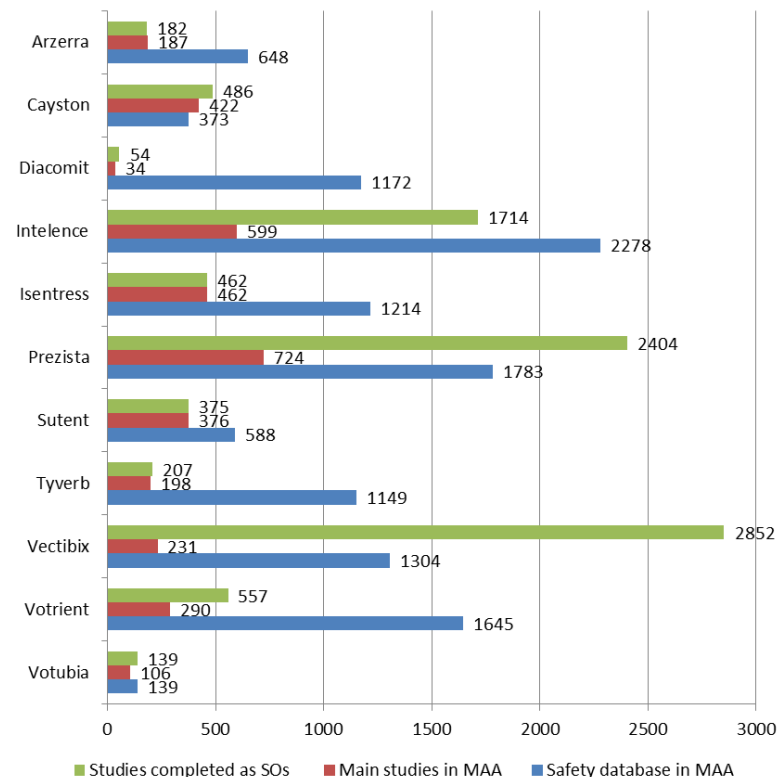
SO data vs. initial data

Duration of median patient follow-up in SO studies vs. the follow-up duration in MAA data (N=77)



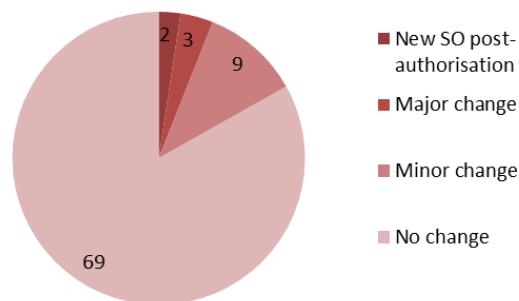
Post-authorisation data required for comprehensive evidence was typically with longer duration / follow-up and in a similar or larger sample size.

Number of subjects receiving CMA product in main studies and safety database at the time of MA and in studies completed as SOs, all CMAs converted (N=11)

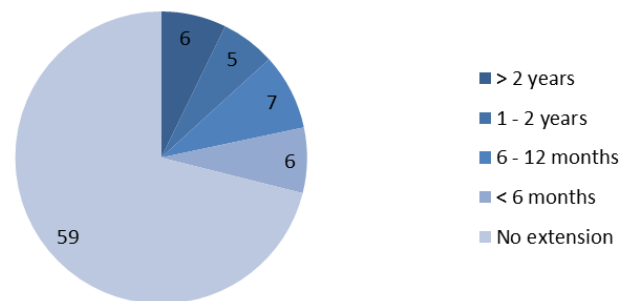


Changes to specific obligations

Changes to scope of specific obligations, all SOs completed or pending, N=83



Extensions of due dates for specific obligations, all SOs completed or pending (N=83)

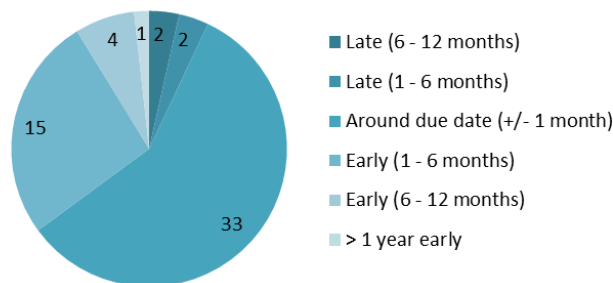


Most specific obligations did not have any change to their scope and due dates. Only very few had major changes to the scope or extensions beyond one year.

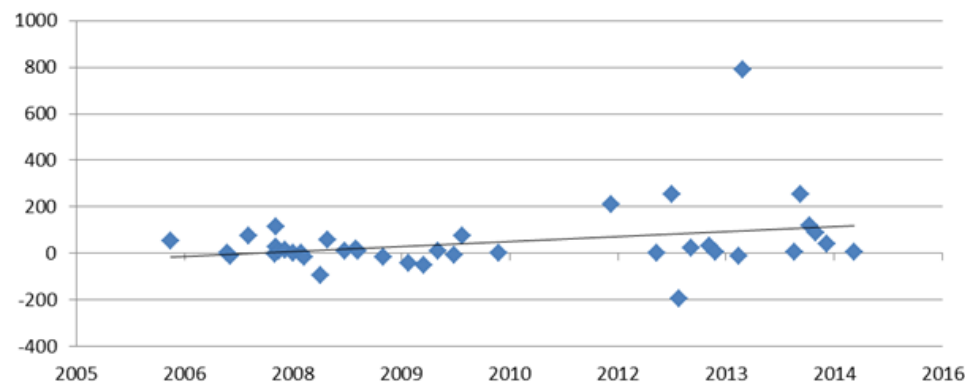
Although often the changes in scope and timelines of specific obligations were related to difficulties in recruitment and study initiation or conduct, in some cases it was linked to better-than-expected outcomes (e.g. lower than expected incidence of metastases or longer overall survival).

Observing the due dates

Submission of SO results in relation to due date
(N=57)



Accuracy of submission (number of days in advance of due date
(delay = negative), arranged by the submission date)



The due dates for submission of data from specific obligations were generally observed and often (33%) data were submitted more than a month early



Thank you for your attention

Further information

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