An Independent Report on the Global Regulatory Approach to Achieve the Development of Safe, Effective and Affordable Drugs for Dementia

Executive Summary and Recommendations

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Introduction

Since Alzheimer's disease was first described in 1906, there is no doubt scientists have made remarkable strides in understanding how Alzheimer's disease and other dementias affect the brain. However, there remains a general view from both patients and regulators that dementia research and development is at a crossroads.

Knowledge gaps in the disease biology, inadequate data-sharing and open science mechanisms to accelerate discovery, coupled with under-optimised clinical trial infrastructure and lack of understanding of regulatory challenges, all lead to slow and inefficient translation of research into the clinical setting and of clinical results back into research.

Context

There is a high failure rate of candidate drugs, predominately in the early stages of development, from the pre-clinical to early development. The medicine regulatory agencies have already begun to think specifically about these challenges and are offering guidance and consultations.

In February 2013[1], the US Food and Drug Administration issued draft guidance addressing trials in early stage Alzheimer's disease. Throughout 2015 the European Medicines Agency and the Pharmaceutical and Medicines Devices Agency of Japan will revise its own guidance.

Methodology

A structured three-part work programme has been undertaken with clinical-scientific experts and medicine regulators, to collectively evaluate approaches using existing laws and regulations in the most optimal way.

Part I identified research and development challenges in dementia drugs. Part II was to work with key regulatory agencies and researchers on the research gaps and development challenges. Part III is to establish a common understanding at the global level that will address the challenges and create new opportunities in drug development.

[1] http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM236689.pdf

Discussion

There is increasing pressure from patients who are willing to take more risks as a result of having no other alternatives. However, this is balanced against the very real risk of causing people significant harm. The current regulatory framework allows – under certain circumstances – for the granting of a marketing authorisation for a medicine where uncertainties remain about the benefit-risk balance, provided that the medicine meets an unmet medical need and early indication of efficacy.There is a question around whether in order to get a drug to patients; international regulators should secure "policy cover" to say in advance that there is a collective will to take these risks. This would allow the products to go to market earlier, but with the publicly accepted proviso that if patient safety is compromised, the regulators will take these products off the market.

Recommendations

Recommendation 1: Learn from attrition analysis and reconsider molecules previously rejected by pharmaceutical developers, if the science could be viewed differently.

Recommendation 2: Support the regulators who have identified and agreed a way forward on six areas of work throughout 2015 notably in relation to clinical trial efficiency, modelling and extrapolation and composite endpoints.

For further information www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency

Recommendation 3: Coordinate existing pathways that are conducive to current gaps in science within existing laws and procedures that can be achieved in the context of different regulatory pathways.

Recommendation 4: Spearhead adaptive clinical development by focusing on accelerated regulatory pathways for dementia medicines. Employ a sensitive and patient centric approach to risk-benefit ratio, learning from other diseases like HIV, oncology and rheumatoid arthritis and assessing applicability to dementia.

Recommendation 5: Create a multilateral advisory platform of regulators and research experts who can leverage and integrate the outcome of the above recommendations for dementia drug development.