Synergistic Effects - A New Approach in Combination Therapy

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At the end of all drug research stands the “approval of the (new) drug”. Therefore, it is un-avoidable for scientists to think about the process of regulation although during the development. Textbooks are full of negative interactions effects of medicines in in combination treatment, but due to lack of ethic to make RTCs, mainly discovered by chance. The result over years, common knowledge of classical pharmacology is: “Avoid Combination!” Moreover, to be frank, there have been and are several inacceptable combinations on the market. If new ideas like “synergy” comes up – among regulators – in “slow motion”.

A major argument was that different ingredients of a fixed combination could have different courses or durations of action, e.g. the synchronization of the bioavailability of the substances. However, this is only convincing, if the mode of action is needed simultaneously, not, if there are different targets etc. Nevertheless, even in therapy with chemically defined medicine, we are reaching borders.

First: There are serious diseases, from which since a long time, is known that they cannot sufficiently be influenced (or cured) with one drug alone. In addition, in the last years the disease needing combination-therapy increased.

Second: The ageing society brings up more and more “multi-morbidity” patients needing polypharmacy where the influences of different drugs to each other are mainly unknown but the combination is unavoidable, caused by the severity of the diseases. It’s typical that problems arises, when new or additional medicines are needed, or different physicians, not knowing from each other prescription, prescribe different drugs.

Third: In the fighting with bacteria etc., we are close to the end of effective antibiotics. We urgently need new substances OR new ideas of treatment; less side effects and eradication should result in less resistance. However, up to today this is only a dream.

Fourth: We have many problems with (tropical) diseases e.g. in Africa. Of course, we have some effective (chemically defined) medicines e.g. against malaria, but in poorer countries they are too expensive and we need (cheaper) alternatives, e.g. plants like Artemisia annua.

Combinations are used commonly for many different indications. To cover all the individual needs of the patients a wide range of different combinations with different content of active substances need to be marketed.

New pathways for the authorisation of combinations need to be introduced. The next logical step in the regulatory framework is the co-approval of combination therapies based on targeted approaches, which so far does not exist. The approach introduced in this thesis recommends this additional new way of drug approval to overcome this gap. The development and approval of novel therapeutic concepts would be a consistent step towards a better health care. A clear regulatory pathway towards an approval of drug combinations could help agencies, health care professionals and patients to gain safer therapies and clear recommendations for medical practice.