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Reply to comment on: Mumme M, et al. Tissue engineering for paediatric patients. Swiss Med Wkly. 2019.149.w20032

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Rose et al. [1] add some important points on the difficulties of paediatric regulations and medical and therapeutic meaningfulness. We thank them for their interest and contribution on the topic and we find ourselves mostly in agreement with their comments. Following is a concise reply to the most critical raised points.

1. We agree that the phrase "children are not small adults" does not reflect the complexity of the different stages of maturation from newborn to adult. Moreover, whereas treatment concepts for bodily mature adolescents are comparable to those of young adults, there is evidence that maturation with respect to physis fusion is even happening earlier in children today as compared with former generations [2]. Thus, a legal cut-off at 18 years is not substantiated physiologically in many cases. Nonetheless, expected diseases and injuries encountered in the paediatric population are generally not identical with those of adults. In this respect, in our opinion the key message that different treatment concepts need to be considered and possibly applied in different age groups remains valid.

   With regard to application of advances therapies in cartilage repair, Rose et al. claim microfracture to be inferior to ACT [3]. The reference (Gudas et al.) cited to support this statement deals with a randomised controlled trial comparing one-step osteochondral autograft transplantation (OAT) in an age range of 15 to 40 years. The paper does not refer to autologous chondrocyte transplantation (ACT). For the comparison of ACT vs microfracture, several randomised controlled trials were published with still controversial results. Benefit for patients is expected in lesions bigger than 2.5cm^2 or in high sport activity [4]. For children and adolescent patients satisfactory results are published [5], but high level of evidence studies are lacking.

2. The criticism that paediatric investigation plans are not guided by therapeutic intention but by regulatory logic and tunnel vision might be correct for some cases. We believe it is very important that sponsors and investigators develop the paediatric investigation plan based on medical and ethical considerations. If an unnecessary burden or even possible harmful effects for paediatric patients is feared, these considerations should be openly discussed with the regulatory bodies and investigation plans revised or amended. The ethical commission should be the authority to guarantee a justifiable risk benefit ratio.

3. We agree that fixed legal age limits are probably too simple for a reasonable testing of medicinal products in different physiological conditions and medical indications. However, the defined legal age limits do not take from the investigators the responsibility to design a sound study protocol reflecting the different needs in different age groups beyond legal definitions. The target age groups and related comparator treatment need to be carefully selected for the respective indications.

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