would probably not have arisen if all our original figures and the text were retained in the final published article (the figures have to be removed because of space constraints). Nevertheless, we have tried to address the concerns here:

1. The major outcome variable of our study was the amount of native bilirubin left over after exposure to light. We consciously avoided using the amount of isomers formed as the primary outcome variable as we did not characterize them. We therefore used the term photoconversion rather than photodegradation or photoisomerization. On the other hand, we would also like to point out that the technique used by us (LC-MS/MS in a highly efficient Multiple Reaction Monitoring mode [MRM] along with hydrophilic interaction chromatography) separates bilirubin from its isomers having similar molecular weights. So, we do not agree with the reader's comment that we 'focused largely on photodegradation and not photoisomerization'.

2. We agree with the reader that the photochemistry of bilirubin in organic solvents could be different from serum/aqueous albumin solutions. Still for the comparative evaluation of different light sources under controlled experimental conditions, we opted for the methanolic solution of bilirubin at the concentration of 1μg/ml because of the following factors: (*a*) lack of aqueous solubility of bilirubin (*b*) concerns over availability of unbound fraction of bilirubin from plasma for photoreactions and (*c*) the risk of interferences in estimation by the biomatrix. Usage of organic solvents for water insoluble drugs for photodegradation analysis is not uncommon. For the preparation of stock concentration of bilirubin, dilute ammonia solution of methanol was used and it was serially diluted to reach the concentration of 1μg/mL with methanol.

3. It is true that over-irradiated samples are capable of producing more and more photoconversion products. However, the method adopted by us for determination of bilirubin concentration (LC-MS/MS) is the gold standard for measuring compounds with higher precision. As it is quantifying the compounds based on their molecular weight, color of the compound is immaterial. The standard methanolic bilirubin appearing at 1.23 min and the formation of a photoisomer product at 1.9 min can very well be seen in the accompanying **web figure.** Moreover, we have used more time points for quantification.

4. We have shown the separation of peaks within the period of 3 min in LC-MS/MS using the method reported in the manuscript (Figure available on request). For *in vivo* quantification process (ongoing study), the method was optimized to include the extraction solvent with an internal standard in the composition of 70% acetonitrile containing 0.1% formic acid. Therefore, the same method was adopted for this in vitro study. From the observed data using the method, it is convincing that the photoisomers formed and survived the experimental conditions. However, we did not isolate any photoisomer for further characterization. Further studies are in progress to isolate and characterize the photoisomers for their quantification *in vivo* conditions.

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Short course of Antibiotics in Neonatal Sepsis

It is appreciable effort on part of Saini, *et al*. [1], to cut short the usage of antibiotics in case of culture negative "sepsis" but we have some observations regarding the study.

A complete sepsis screen score should have been taken into consideration before deciding to start the antibiotics. CRP alone with clinical suspicion will lead to falsely high number of neonates getting enrolled which will affect the primary outcome as these 'false positive' cases are less likely to present with' treatment failure [2]. Sepsis score not relying upon 'CRP alone' would have been more useful as this costly test is not universally available, as mentioned by the authors also.

Babies falling sick within fifteen day period are presumed to be the continuum of initial episode while a re-infection or sepsis caused by different organism cannot be ruled out completely. The number of neonates who were labeled as 'treatment failure' will be inflated falsely because of re-infection/fresh sepsis. It is not possible to ensure equal distribution of these fresh cases in both groups as sample size is very small. So the

conclusion drawn that the short course antibiotics is not harmful can not be validated adequately even by this pilot study.

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REPLY

The diagnosis of neonatal sepsis using a "sepsis screen" is not as simple as it sounds. Two systematic reviews have concluded that although none of the standard sepsis screen parameters (or combinations thereof) is satisfactory, CRP is the best individual parameter. It is for this reason that we opted for CRP alone. CRP is widely accepted and used and the objection about it's "high cost" is an individual viewpoint. It is true that fresh cases of culture-negative sepsis may get incorrectly included as "treatment failure" and may not necessarily get evenly distributed despite randomization. This is an unavoidable risk in a pilot trial. We have not concluded that a shorter duration of antibiotics should become a standard of care. We have only suggested that on the basis of this small study, a large definitive non-inferiority trial could be planned.

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Short Course Antibiotics in Neonatal Sepsis

We have a few comments on the recent article by Saini, *et al*. [1]. The attempt to investigate the shortest possible duration of antibiotics in probable neonatal sepsis is appreciable as it will lead to decreased economic burden, hospital stay, and adverse effects associated with treatment.

The Table II showing comparison of co-interventions, number of neonates receiving CPAP and number receiving conventional oxygen shows statistically significant difference in the two groups [1]. More invasive procedure can lead to more chances of introduction of fresh sepsis in otherwise culture negative non sepsis children. This could be one of the reasons behind more cases presenting with treatment failure in the group receiving antibiotics for 7 days as more number of children in this group incidentally received CPAP.

The basis of choosing fifteen days as cut off time for following up neonates after completion of antibiotics has not been explained.

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REPLY

It may be true that more co-interventions in the 7-day arm have resulted in slightly higher treatment failure rate. However, two facts need to be considered before one prematurely draws conclusions. Firstly, the difference in failure rates between the short-course and the 7-day treatment arms was not statistically significant. This means that the "difference" was likely due to a chance phenomenon and one must not read too much into it. An appropriate sample size may well have thrown up an insignificant difference or significantly higher rates in either of the groups. Secondly, in a randomized controlled trial, all post-randomization events whose distribution is significantly different are either associated with the intervention or are chance phenomena or are biased associations. Thus, differences in co-intervention rates (*e.g.* CPAP) could be related to the duration of antibiotics *per se* or chance or related to a performance bias (this being an unblinded trial). Thus, we feel it is premature to make a direct association between a co-intervention that happened to be statistically different and an outcome that showed no significant difference.

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