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Oral presentation

O123 To overdose or underdose? The question of Kaletra in children in the UK/Irish Collaborative HIV Paediatric Study (CHIPS)

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Background

The licensed lopinavir/r paediatric total daily dose is 460 mg/m2 without, and 600 mg/m2 with concurrent NNRTIs. The 460 mg/m2 dose without NNRTIs was chosen in preference to 600 mg/m2 in a post-hoc drug-interaction analysis [1]. Excellent VL suppression was also reported (79% <400 c/ml at 48 wks) but was based on the higher 600 mg/m2 dose. Thus, some paediatricians prefer this higher dose regardless of concomitant NNRTI therapy.

Methods

We calculated lopinavir/r doses (mg/m2) prescribed without NNRTIs in the UK/Irish CHIPS cohort from 2000–2007, every time height/weight was measured. We investigated predictors of current dose, including sex; VL and CD4% at the previous visit, current age, CDC stage, height/weight-for-age, calendar year, formulation, frequency and previous PI using mixed models with random effects for child and centre. We considered whether current lopinavir/r dose predicted the next VL being <400 c/ml using binomial mixed models.

Summary of results

311/1,336 (25%) children in CHIPS had ever taken lopinavir/r without NNRTIs, total 654 child-years. Median age at lopinavir/r initiation was 9.0 years (IQR 5.1–12.1). 684 doses were recorded in 299/311 children: 52% were syrup, 38% capsules and 10% tablets, with only 3% once (rather than twice) daily. Dose/m2 could be estimated 2,748 times in 278 children: few (6%) were >10% below the 460 mg/m2 target, and few (9%) >10% above the 600 mg/m2 target, with most >410–<530 mg/m2 (46%) or >530–<660 mg/m2 (39%). In a multivariable model, doses were 17 mg/m2 [95%CI 0–34] higher in children who had prior AIDS, 2 mg/m2 [0–3] higher for every log10 higher VL at the previous visit, 48 mg/m2 [38–58] higher with capsules/tablets vs. syrups, 22 mg/m2 [4–40] higher with twice- vs. once-daily dosing, 19 mg/m2 [15–24] and 10 mg/m2 [6–14] higher for every one unit lower current weight- and height-for-age, respectively, and 9 mg/m2 [5–14] higher for every year younger under 10 ($p < 0.05$). Dosing varied widely by centre. Adjusting for age, there was no strong evidence that higher doses increased the chance of the next VL being <400 c/ml (OR = 1.10 [0.96–1.25] per 50 mg/m2 higher, $p = 0.16$) or <50 c/ml (OR = 0.82 [0.73–0.91], $p < 0.001$).

Conclusion

In summary, younger or stunted/wasted children or those with prior AIDS/higher VLs received higher doses. Doses were higher with capsules/tablets, likely reflecting over- rather than under-dosing when solid formulations cannot achieve exact doses. However, we found no clear evidence that higher doses improved VL suppression.

References

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