Letter

# Timing of drotrecogin alfa (activated) treatment in severe sepsis

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The effect of the timing of drotrecogin alfa (activated) (DrotAA) treatment on the outcome of severe sepsis was recently evaluated, using the integrated clinical trial database INDEPTH. The evaluation demonstrated an association between earlier treatment (i.e. treatment within 24 hours of the appearance of first organ dysfunction) and lower patient mortality [1].

We assessed the timing of DrotAA treatment in our own (mixed) intensive care unit over a 3-year period. We selected all patients treated with commercial DrotAA since its availability in The Netherlands. Patients were treated with DrotAA according to the national guidelines [2].

As the results presented in Table 1 show, patients treated within 24 hours were younger and more often had pneumosepsis (45% versus 9%, $P = 0.03$), which was due to community-acquired pneumonia in 12 out of 14 cases (86%). *Streptococcus pneumoniae* was the most frequently involved pathogen in these pneumonia patients (seven of 12 cases, 58%). Notably, and in contrast to the analysis of the INDEPTH data, hospital mortality rates were comparable

**Table 1**

**Baseline patient characteristics based on the time to treatment**

| Parameter | 0–24 hours ($n = 29$) | >24 hours ($n = 11$) | *P* value |
|---|---|---|---|
| Age (years) | 51.5 ± 17.6 | 67.4 ± 9.9 | 0.008[a] |
| Male sex | 13 (45%) | 3 (27%) | 0.31[b] |
| Acute Physiology and Chronic Health Evaluation II score | 23.9 ± 5.5 | 26.9 ± 9.8 | 0.22[a] |
| Time from first organ dysfunction to start of treatment (hours) | 12.2 ± 6.8 | 45.7 ± 21.8 | <0.0001[a] |
| Number of organ dysfunctions | 3.6 ± 1.2 | 3.3 ± 1.3 | 0.55[a] |
| Mechanical ventilation | 25 (86%) | 11 (100%) | 0.19[b] |
| Vasopressors | 28 (97%) | 10 (91%) | 0.47[b] |
| Recent surgery | 8 (28%) | 6 (55%) | 0.13[b] |
| Primary site of infection | | | |
| Respiratory system | 13 (45%) | 1 (9%) | 0.03[b] |
| Abdominal | 8 (28%) | 5 (45%) | 0.28[b] |
| Urogenital | 2 (7%) | 2 (18%) | 0.29[b] |
| Other | 6 (2%) | 3 (27%) | 0.66[b] |

Data presented as mean ± standard deviation or as *n* (%). [a]Student's *t* test. [b]Chi-square test.

DrotAA = drotrecogin alfa (activated).

between early treatment and late treatment (38% versus 36%, $P = 0.93$).

In this small study evaluating DrotAA treatment practice in our intensive care unit, patients treated earlier were younger and more often had community-acquired pneumonia. Given that patients with community-acquired pneumonia seem to benefit most from DrotAA treatment [3], it would be interesting to identify differences in primary sites of infection between early treatment and late treatment within the INDEPTH data.

## Authors' response

Jean-Louis Vincent, James O'Brien Jr, Arthur Wheeler, Xavier Wittebole, Rekha Garg, Benjamin L Trzaskoma and David P Sundin

We thank Dr Choi and colleagues for their interesting comments. We checked the database with Eli Lilly, and we found no differences in the sources of infection according to the timing of intervention.

## Competing interests

The authors declare that they have no competing interests.

## References

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