

Keeping abreast of progress for the benefit of public health (including filling in knowledge gaps): US Regulator's perspective

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Keeping abreast of progress

- As previously discussed, the TOUCH program permits us to be aware of the incidence of PML in what is essentially real time
- By itself, of course, these aren't research results, but it permits rapid actions of various kinds
- This also permits information sharing with our European colleagues



Keeping abreast of progress

- Routine and “special” interactions with EMA (in person, video conferencing) permit discussion of bases of regulatory activities (labeling changes, etc.)
- We have begun to have a more regular interaction with our EMA colleagues
- It helps to get to know colleagues (exchange program?)
- We have met with the PML consortium to discuss various issues related to exploring the mechanisms of PML production



Knowledge gaps

- Essentially all patients with PML are treated with plasma exchange (PLEX)
- Many such patients get Immune Reconstitution Inflammatory Syndrome (IRIS), and are treated with steroids
- Some of the deaths have presumably been due to IRIS
- We do not know if PLEX is useful in treating PML, or if current treatment of IRIS is effective
- Are there more effective, safer PLEX regimens?



Knowledge gaps

- Other treatments of PML are being tried
- We don't know if they are effective
- We may not even know they are being tried
- We don't know how to study this
- Agency experts in anti-viral treatments should be involved in the effort



Knowledge gaps

- As discussed yesterday, we are currently evaluating all relevant information about patients with PML
- This evaluation may identify not only other risk factors for the occurrence of PML, but characteristics of patients that predict the course of PML, response to treatment, etc.



Knowledge gaps

- An initial preliminary look at the data suggests that a higher percentage of patients in the US die from PML compared to those outside the US
- Why is this?



Knowledge gaps

- Although it is difficult to know how to perform adequately controlled trials of treatments for PML, the identification of biomarkers may help; in particular, they may help identify ineffective therapies *quickly*



Funding

- As noted yesterday, PML may be considered an orphan disease
- There is a grant mechanism for controlled trials of orphan conditions
- This option may be worth exploring



Communication

- As we have heard, there is a desire for more information to be available in real time to both prescribers, patients, and families
- Although the mechanisms for doing so may not be immediately obvious, it is worth discussing with the interested parties, what information would be useful, and possible ways to get it to the people who need it

