

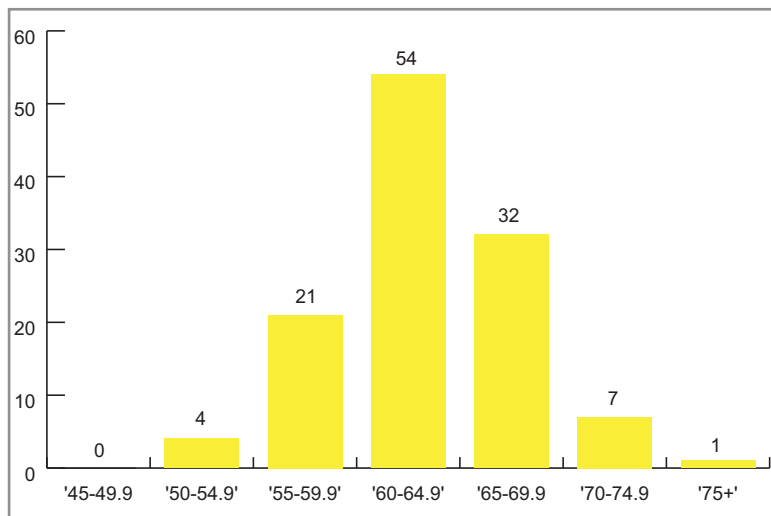
ECORN-CF: www.ecorn-cf.eu

Editorial, by Jeannette E. Dankert-Roelse

Benchmarking

In the December 6, 2004 issue of "The New Yorker" the surgeon and writer Atul Gawande, famous for his critical writing about how doctors perform but at the same time providing tools how to improve performance and achieve the best possible quality in patient care, wrote a noteworthy article about CF-centre care in the USA.

The results of CF-centre care in the USA appeared to vary much more than one would expect. As Gawande put it: you would expect that "a graph showing the results of all centers treating cystic fibrosis (...) would look something like a shark fin, with most places [centers] clustered around the very best outcomes (...) [but] what you tend to find is a bell curve: a handful of teams with disturbingly poor outcomes for their patients, a handful with remarkably good results, and a great undistinguished middle".



*Lung Function in Adults,
 US CF-centres 2008*

In his article Gawande describes how one CF-centre with results well below the average started actions to improve their results. They did that by being more open about how they were doing. This first action - and the article in "The New Yorker" - started a small revolution in the registration of the results of US CF-centre care. Nowadays, it is possible to find the results of each centre on the site of the CF foundation while until 2006 the results were shown only anonymously. During the last NACF conference a number of CF-centres showed how their results improved by learning from the better performing centres.

Benchmarking is not new for ECORN-CF.EU; our leading motto is "Learning from the best".

In this newsletter more results are reported from the last Quality Round Table, the next step is indeed to learn from the best, and the introduction of the Question/Answer of the month is put in the spotlight. The last newsletter of ECORN-CF.EU in it's present form is planned to be published at the beginning of May 2010.

Benchmarking 1
 Question of the month 2
 Action items as agreed during the 4th Quality Round Table 4

Question of the month

During the last Quality Round Table in Prague, in October 2009, a number of selected questions were discussed. The questions were selected because the answers aroused much debate or because it was a very new topic, e.g. questions about the swine flu. When these questions were discussed it appeared that sometimes, although the answer had evoked much debate, the answer could be found easily in the ECFS consensus documents that were selected to be the ECORN-CF guidelines for answering the questions.

By discussing the questions all participants of the meeting became aware again that when answering questions the designated consensus documents or guidelines should be used and that, when a debate arises, one should point out these guidelines had been leading for the answer. On the other hand, there were questions that were not so easy to answer because no guidelines are available yet, or the guidelines do not provide an answer for this specific question or the guideline seems to be outdated already. Therefore a proposal was made to select a question of the month from all questions sent to ECORN-CF for which already an answer was written and to send this QA pair to all participants of ECORN-CF.

How and by whom is the question of the month selected?

Annette Pfalz contacted several ECORN-partners from the local expert advices with most questions, i.e. Germany, Belgium/the Netherlands, Czech Republic and United Kingdom. Kris de Boeck (Belgium) who did the proposal of the QA of the month in Prague already offered to do the first "QA of the month" which was sent around in December 2009. Daniela d'Alquen (Germany) prepared the issue for January 2010 and the latest "QA of the month" about "Vertex-770 potentiator" for this month was prepared by Judy Bradley (UK).

The experts choose the questions themselves. All QAs have already been published in the Central Archive (in English) and are available on the website (go to www.ecorn-cf.eu and then click on "Central Archive"). After consultation with the project leader, Prof. Dr. Thomas O. F. Wagner, and with his agreement the text is put into a "QA of the month" template and sent to all experts.

From which questions is the question of the month selected?

So far, all "Questions of the month" were already published in the Central Archive, but this was not a pre-requisite.

What criteria are used when selecting a question of the month?

An important criterion for selection is that the QA should ideally be about a topic that interests the majority of the CF specialists. If possible, the answer should be one that took quite some time to pick and select the information from several articles. In other words: not an answer that could be found easily in a CF compendium or in the guidelines. The idea is that many persons can benefit from the work done by the expert who spent quite some time to find all the relevant data for the answer.

Is the question of the month only sent to the partners or is it also published on the website?

The QA of the month is only sent to all official experts of ECORN-CF (about 90); but it can be found again on the website as it is published already in the English Central Archive.

How do the partners appreciate the question of the month?

The QA of the month seems to be a good tool to make experts who only rarely answer questions aware that they are part of ECORN-CF. Furthermore, it is a nice knowledge update that does not take much time for each expert.

After the question "CF and the desire to have children" became QA of the month in January a comment was made that the original answer was a bit against the internal guidelines about not being too specific (the answer was very specific). Therefore, an additional comment was written that was published in the archive and in the original German QA. The questioner was also informed about the update. This was possible because the question was not asked anonymously but after the questioner had logged-in.

Summarizing, the initiative of the QA of the month seems to be a success as the experts can identify QAs that were not easy to answer without much effort; moreover, by putting such a difficult QA in a spotlight it evokes reactions that may lead to more balanced answers and finally it attends the ECORN-partners on new developments in CF-care and research.

If you have any questions regarding the QA of the month, please ask Annette Pfalz:
pfalz@em.uni-frankfurt.de

In the textbox an example of a QA of the month is shown.

Question

Vertex-770 potentiator

Dear expert team, my son's genotype is DF508 and R347P. As VX-770 only studies effectiveness in G551D (and DF508) at the moment I wonder what the III-V) mutations with a certain functionality of the probability is that this drug also works for other (class CFTR protein (my son must have some functionality as he is pancreatic sufficient). I guess that further studies have to be done but I would like to understand the working method of the drug and if it can be applied to other mutations. I would also like to understand why the company only focus on one specific mutation. Thank you.

Answer

Dear Questioner,
 This is an excellent question.

The answer is, however, somewhat complicated.

1. VX-770 is a small molecule "potentiator" which can increase chloride transport via defective CFTR. This effect is most pronounced in individuals with the class III mutation G551D.
2. In vitro (in a test tube) there is data which suggests that VX-770 has activity on R117H mutant CFTR (a class IV mutation). We have not been able to find published data on the less common Class IV mutations, such as R347P. This does not mean these data do not exist. There is a strong possibility that some level of activity will be seen on other mutations in this class.
3. To study a drug in a clinical setting (and thereby bring a drug to market) narrow parameters are required such that conclusive data can be generated. As G551D is the third most common mutation in CF and that in which VX-770 has most potent activity, it is logical to study the agent initially in this setting (although studies in dF508 homozygotes are also underway).
4. Should clinical studies prove this agent to be effective it will likely receive approval for clinical use in late 2012 or 2013 (accelerated, owing to its orphan drug status).
5. Positive data for VX-770 in individuals with G551D mutations will result in researchers looking at other mutations for potential efficacy. The same rigorous study clinical design would neither be required nor necessary to support this use. This can then prompt "off-label" use of these products in certain, appropriate clinical scenarios.

In summary, while the current VX-770 study design may look somewhat exclusionary – this is required to give the best opportunity for this new product to demonstrate efficacy in stabilizing the clinical course of CF. This is the necessary process involved in bringing drugs to market (not just in CF). Should positive results be obtained for VX-770 in those with G551 D mutations we will be looking for opportunities to expand its use in other mutations in which clinical benefit might be predicted based on laboratory data. Analogously, TOBI and DNase were both studied in very strictly defined populations, but physicians use this "licensed product" in a much more broad capacity guided by both on going research in new situations and clinical experience.

*Thank you for your inquiry.
 Best Wishes,*

Action items as agreed during the 4th Quality Round Table

1. Fine scoring

During the discussion about the fine scoring of the QAs it seemed that some scorers tended to give high scores while others tended to give lower scores. Therefore it was agreed that Daniela d'Alquen would look at the scores of the individual scorers and compare the inter-scorer-variability. The results of these analyses are shown in the Tables 1 and 2.

Table 1. Inter- and intra-individual scorer variability for content quality

Content Quality	% Q/As (n=70)			
	≥2 pts<median	>1pt< median	>1pt>median	≥2 pts>median
Scorer 1	20,3	10,1	8,7	2,9
Scorer 2	14,3	5,7	15,7	7,1
Scorer 3	13	11,6	4,3	7,2
Scorer 4	1,4	5,7	7,1	25,7

Table 1. Inter- and intra-individual scorer variability for formal quality

Formal Quality	% Q/As (n=70)			
	≥2 pts<median	>1pt< median	>1pt>median	≥2 pts>median
Scorer 1	28,6	18,6	0	0
Scorer 2	0	5,7	7,1	0
Scorer 3	7,1	14,3	4,3	1,4
Scorer 4	0	0	25,7	10
Scorer 5	2,9	7,2	23,2	8,7

The following conclusions can be drawn

- The tendency of a single Scorer to score lower or higher is consistent for content and formal quality.
- Scorer 1 scores clearly lower than the median, especially concerning the formal quality.
- Scorer 2 scores relatively balanced: the scores for content quality are often lower but also often higher than the median scores; the formal quality is always near the median.
- Scorer 3 scores more often lower than higher, so has a tendency to score lower than the median.
- Scorer 4 scores clearly higher than the median, very seldom lower, concerning the formal quality the scores are never lower than the median.
- Scorer 5 has a tendency to score higher than the median.

2. Check how many answers are changed before they are published in the Central Archive and how many answers are changed for each language group.

The results of this action item are shown in Table 3.

Table 3. Total number of questions (until 22/12/2009) subdivided for quality

Country	Total N Q/As	Quality good, N(%)	Quality with flaws, N	Quality not acceptable, N	Changed answers, N
Germany	305	284 (93)	20	1	21
Czech Republic	48	39 (81)	8	1	9
UK	29	28 (97)	0	1	1
Romania	16	7 (44)	7	2	9
Lithuania	18	11 (61)	7	0	7
NL / Belgium	66	65 (98)	1	0	1
Poland	14	9 (64)	5	0	5

3. Inform the language groups about the results of the fine scoring

Daniela d'Alquen sent the results of the fine scoring to all ECORN advice expert partners indicating which answers were not satisfactory and why.

Contacts

ECORN-CF project leader:
Prof. Dr. Thomas O.F. Wagner

Annette Pfalz (coordination and administration)
Pneumologie/Allergologie (Prof. T.O.F. Wagner)
Medizinische Klinik 1 / Haus 15 B
Klinikum der Johann Wolfgang Goethe-Universität
Theodor-Stern-Kai 7
D - 60590 Frankfurt am Main

Tel +49-(0)69-6301-3824
Fax +49-(0)69-6301-6335
E-mail info@ecorn-cf.eu

Public relations work package leader:
Dr. Jeannette E. Dankert-Roelse
Kindergeneeskunde
Atrium Medisch Centrum
Postbus 4446
6401 CX Heerlen

Tel +31 45 5766931
Fax +31 45 5767154
E-mail SRS07@atriummc.nl