THE LAST WORD:

ICER's review of Anti-B-Cell Maturation Antigen CAR T-Cell and Antibody Drug Conjugate Therapy for Heavily Pre-Treated Relapsed and Refractory Multiple Myeloma

In its Final Report for multiple myeloma therapies, ICER announced that two of the therapies it reviewed had low long-term values at current prices. These included idecabtagene vicleucel [ide-cel] (Abecma) with a recommended price discount of between 37% and 54%. At current prices ICER issued an affordability and access alert, which contradicted its claims for discounting pointing out that at its imaginary budget impact threshold that some 43% of eligible patients could be treated with ide-cel and 50% with ciltacabtagene autoleucel [cilta-cel] (under FDA review) within five years. These results should not be taken seriously.

ICER's final evidence report illustrates once again how out of touch ICER and their academic modeling advisors, in this case from the University of Colorado Anschutz Medical Campus, actually are in their failure to recognize the standards of normal science in their commitment to the invention of imaginary evidence.

If claims for competing products in multiple myeloma are to have any credibility they must be open to empirical evaluation. ICER makes no claim; instead, ICER's recommendations appear designed to obscure deliberately any attempt at empirical assessment in their reliance on assumption-driven simulation models, which defy both logic and standards for measurement. As such, as noted on previous occasions, the ICER models are a sham. ICER might claim that they are following standards in health technology assessment that are widely recognized. If so, those who subscribe to this belief in creating approximate evidence rather than hypothesis testing should reconsider: "truth" for ICER is consensus on constructing imaginary evidence.

The claims generated from the multiple myeloma ICER modeling rest on the notion of a quality adjusted life year (QALY) to support incremental cost-per-QALY claims and mythical cost-per-QALY thresholds. Take these away and the model collapses along with ICER's business case. The ICER model rests on a failure to understand the levels of evidence, the axioms of fundamental measurement, on which physical science and mature social science rest.

ICER holds to a quaint belief that the various preference instruments that support the creation of values and utilities have ratio properties; or at least they have hidden ratio properties known only to the experts. For a measure such as height and weight to be able to support arithmetic operations it must have a true zero; no observation in capturing height or measuring weight can have negative values – that is, values less than zero. This allows multiplication and

division, as well as addition and subtraction, which, in turn, mean the measure must have equally spaced distances between scores (an interval property).

ICER dismisses these annoying characteristics and insists, without providing any proof, that all preference measures have ratio properties. That means they can support a QALY by multiplying time in a disease state by a value or utility score which has a true zero and is on a range 0 = death and 1 = perfect health. There is, unfortunately, a fly in the ICER ointment. We have known for over 30 years that when patients respond to these outcome instruments that they can value states as worse than death; they produce negative scores. Now, unless ICER has produced the most innovative contribution to measurement theory for over a century – a ratio measure without a true zero – the QALY modeling collapses.

In the multiple myeloma report utilities are taken from an unpublished conference presentation (which has therefore not been subjected to peer review) that uses the EQ-5D-5L instrument. That is, the instrument has five symptoms listed and five response levels within each symptom. We know this instrument creates negative values and has done so since its introduction in 2009. The instrument was intended to replace the EQ-5D-3L, introduced on the grounds that it might be a more responsive scale. The result has been a disaster, with its use in modeling banned in the UK by the National Institute for Health and Care Excellence (NICE). A recent study found that for five countries, the number of states worse than death valued by respondents ranged from 9% to 32%. None of these issues are raised in the multiple myeloma report – we are led to believe the measure has ratio properties.

Clearly, ICER and its consultants have a deeply held belief in the ratio scale with negative values. Certainly, they should not be disabused of this as long as they make clear the fact that states worse than death do exist. They might also point out that this invalidates their modelling and any claim for relevance in pricing and access recommendations.

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