

# On cost-effectiveness analysis, quality-adjusted life years, and cost-effectiveness threshold values of gemcitabine plus nab-paclitaxel versus gemcitabine alone in metastatic pancreatic cancer in the French setting

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Dear Editor,

While I gratefully acknowledge Demaziere et al.<sup>1</sup> for quoting a publication I coauthored,<sup>2</sup> I would like to discuss three points their interesting article raised.

In cost-effectiveness analysis (CEA)<sup>3</sup>, cost and effectiveness should be reported as mean,<sup>4</sup> not median (see p. 10, Table 3<sup>1</sup>). This methodological recommendation is based on three pillars. First, in a basic CEA comparing two healthcare programs (like gemcitabine plus nab-paclitaxel (GEM-NAB) and GEM alone), the incremental cost-effectiveness ratio (ICER) is calculated as the difference between the average cost of GEM-NAB versus GEM alone (incremental cost) divided by the difference between the average effectiveness of GEM-NAB versus GEM alone (incremental effectiveness).<sup>2-6</sup> Second, assuming the absence of discounting,<sup>3</sup> when multiplied by the sample size, the mean (but not the median) cost per patient of a given healthcare program gives back its overall cost.<sup>4</sup> Third, healthcare costs follow a positively skewed Gamma distribution, with a long right tail.<sup>7</sup> Therefore, the median of the Gamma distribution is lower than its mean and does not give a true and fair view of the average costs per patient. In addition, the rule of thumb of more than 30 observations for the

central limit theorem to kick in does not apply in the case of non-symmetric distribution.<sup>7</sup> As the cost distribution of medical transportation for GEM-NAB patients (see p. 10, Table 3<sup>1</sup>) does not converge to a standard normal distribution, its median and mean do not (and cannot) overlap. As a result, the median cost per patient (€0) is clearly not a good proxy for the mean cost per patient of that healthcare resource.

I agree with Demaziere et al.<sup>1</sup> that life-years saved (LYS) with GEM-NAB and GEM alone should be weighted by patients' health-related quality of life (also known as utility).<sup>3</sup> The resulting weight is the sum of health-state-specific patients' utility subtracted the disutility due to therapy-related grade 3 and 4 adverse events.<sup>2,3,5,6</sup> This way the difference in quality-adjusted life years (QALYs) between GEM-NAB and GEM alone (i.e. incremental QALYs) can be calculated and a cost-utility analysis (CUA)<sup>3</sup> performed, as previous research quoted by authors did.<sup>2,3,5,6</sup>

The last point refers to the local willingness to pay (WTP) for incremental LYS or QALY gained.

The French Health Authority did not explicitly set any WTP but estimated the value of an incremental LYS (€115,000; 2010 values) indirectly from the value of a statistical life (€3 million;

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2010 values).<sup>8</sup> In addition, other informal threshold values for the same CEA/CUA outcomes have been proposed for France. They range from €30,000 to €50,000<sup>9</sup> and from €147,093 to €201,398.<sup>10</sup>

Both the baseline ICERs (€20,128 and €40,256 per incremental LYS with GEM-NAB) reported by Demaziere et al. (see pp. 10, 11, Health costs analysis<sup>1</sup>) and most of those shown in one-way sensitivity analysis<sup>3</sup> are lower than almost all the aforementioned threshold values.

Therefore, while GEM-NAB is potentially cost-effective for French national healthcare insurance, the uncertainty surrounding this finding should be further investigated via a cost-effectiveness acceptability curve.<sup>3</sup>

## Declarations

### *Ethics approval and consent to participate*

This contribution was exempt from ethical review due to it being a Letter to the Editor.

### *Consent for publication*

Not applicable.

### *Author contribution*

**Carlo Lazzaro:** Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Resources; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing.

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### *Competing interests*

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### *Availability of data and materials*

Not applicable.

### *Declaration of generative artificial intelligence in scientific writing*

Carlo Lazzaro declares that no section of this Letter to the Editor was supported by artificial intelligence.

### *Code availability*

Not applicable.

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