

## ***Supplementary Materials***

### **COST-EFFECTIVENESS ANALYSIS OF HRD TESTING FOR PREVIOUSLY TREATED PATIENTS WITH ADVANCED OVARIAN CANCER IN ITALY**

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## APPENDIX 1

### CHEERS 2022 checklist

|                                                  | Item | Guidance for Reporting                                                                                                                          | Reported in section                                                               |
|--------------------------------------------------|------|-------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| <b>TITLE</b>                                     |      |                                                                                                                                                 |                                                                                   |
| Title                                            | 1    | Identify the study as an economic evaluation and specify the interventions being compared.                                                      | Title page                                                                        |
| <b>ABSTRACT</b>                                  |      |                                                                                                                                                 |                                                                                   |
| Abstract                                         | 2    | Provide a structured summary that highlights context, key methods, results and alternative analyses.                                            | Title page                                                                        |
| <b>INTRODUCTION</b>                              |      |                                                                                                                                                 |                                                                                   |
| Background and objectives                        | 3    | Give the context for the study, the study question and its practical relevance for decision making in policy or practice.                       | Introduction                                                                      |
| <b>METHODS</b>                                   |      |                                                                                                                                                 |                                                                                   |
| Health economic analysis plan                    | 4    | Indicate whether a health economic analysis plan was developed and where available.                                                             | Not reported                                                                      |
| Study population                                 | 5    | Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).                 | Materials and methods:<br>The model                                               |
| Setting and location                             | 6    | Provide relevant contextual information that may influence findings.                                                                            | Materials and methods:<br>The model                                               |
| Comparators                                      | 7    | Describe the interventions or strategies being compared and why chosen.                                                                         | Introduction,<br>Materials and methods:<br>The model                              |
| Perspective                                      | 8    | State the perspective(s) adopted by the study and why chosen.                                                                                   | Materials and methods:<br>Healthcare resource consumption and costs               |
| Time horizon                                     | 9    | State the time horizon for the study and why appropriate.                                                                                       | Materials and methods:<br>The model                                               |
| Discount rate                                    | 10   | Report the discount rate(s) and reason chosen.                                                                                                  | Materials and methods:<br>The model                                               |
| Selection of outcomes                            | 11   | Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).                                                                   | Materials and methods:<br>The model                                               |
| Measurement of outcomes                          | 12   | Describe how outcomes used to capture benefit(s) and harm(s) were measured.                                                                     | Materials and methods:<br>The model                                               |
| Valuation of outcomes                            | 13   | Describe the population and methods used to measure and value outcomes.                                                                         | Materials and methods:<br>The model, Quality of life estimates, Baseline analyses |
| Measurement and valuation of resources and costs | 14   | Describe how costs were valued.                                                                                                                 | Materials and methods:<br>Healthcare resource consumption and costs               |
| Currency, price date, and conversion             | 15   | Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.                                 | Materials and methods:<br>Healthcare resource consumption and costs               |
| Rationale and description of model               | 16   | If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.                  | Materials and methods:<br>The model                                               |
| Analytics and assumptions                        | 17   | Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used. | Materials and methods:<br>Baseline analyses                                       |

|                                                                       |    |                                                                                                                                                                             |                                          |
|-----------------------------------------------------------------------|----|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------|
| Characterizing heterogeneity                                          | 18 | Describe any methods used for estimating how the results of the study vary for sub-groups.                                                                                  | Materials and methods: Baseline analyses |
| Characterizing distributional effects                                 | 19 | Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.                                                      | Materials and methods: Baseline analyses |
| Characterizing uncertainty                                            | 20 | Describe methods to characterize any sources of uncertainty in the analysis.                                                                                                | Materials and methods: Baseline analyses |
| Approach to engagement with patients and others affected by the study | 21 | Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (e.g., clinicians or payers) in the design of the study. | Not reported                             |
| <b>RESULTS</b>                                                        |    |                                                                                                                                                                             |                                          |
| Study parameters                                                      | 22 | Report all analytic inputs (e.g., values, ranges, references) including uncertainty or distributional assumptions.                                                          | Materials and methods: Baseline analyses |
| Summary of main results                                               | 23 | Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.                                | Results: Baseline results                |
| Effect of uncertainty                                                 | 24 | Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.    | Results: Analyses                        |
| Effect of engagement with patients and others affected by the study   | 25 | Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study                     | Not reported                             |
| <b>DISCUSSION</b>                                                     |    |                                                                                                                                                                             |                                          |
| Study findings, limitations, generalizability, and current knowledge  | 26 | Report key findings, limitations, ethical or equity considerations not captured, and how these could impact patients, policy, or practice.                                  | Discussion                               |
| <b>OTHER RELEVANT INFORMATION</b>                                     |    |                                                                                                                                                                             |                                          |
| Source of funding                                                     | 27 | Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis                                          | Funding                                  |
| Conflicts of interest                                                 | 28 | Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.                                               | Competing interests                      |

## APPENDIX 2

### Curves fitting

The methodology followed few steps:

- i) Digitization of the survival data of the Kaplan-Meier curves published in the reference study using Engauge Digitizer software;
- ii) Analysis of digitized data with R and STATA software using the algorithms respectively of Guyot and colleagues [Guyot 2012] and Wei and colleagues [Wei 2017] in order to obtain the "fittings" through the main functions (Weibull, Gompertz, exponential, log-logistic, log-normal, generalized gamma); these algorithms allow to map the digitized curves to Kaplan-Meier data by finding numerical solutions to the inverse Kaplan-Meier equations using information on the number of events and the number of subjects at risk. For a more detailed discussion, refer to Diaby and colleagues [Diaby 2014].
- iii) The most appropriate curves for OS and PFS were selected for each treatment. Statistical validity was assessed through the Akaike information criterion (AIC) and the Bayesian information criterion (BIC) (the lowest, the better fit).

| Olaparib – OS curve |        |        |                |
|---------------------|--------|--------|----------------|
| Fitting             | AIC    | BIC    | Notes          |
| Weibull             | 478.32 | 485.44 |                |
| Gompertz            | 480.57 | 487.69 |                |
| Exp                 | 478.58 | 482.14 |                |
| LogLog              | 475.42 | 482.54 | Chosen fitting |
| LogN                | 475.58 | 482.70 |                |
| GenGamma            | 481.84 | 488.96 |                |

| Olaparib – PFS curve |        |        |                |
|----------------------|--------|--------|----------------|
| Fitting              | AIC    | BIC    | Notes          |
| Weibull              | 592.99 | 600.11 |                |
| Gompertz             | 591.99 | 599.11 |                |
| Exp                  | 591.40 | 594.96 |                |
| LogLog               | 586.11 | 593.23 | Chosen fitting |
| LogN                 | 586.92 | 594.04 |                |
| GenGamma             | 588.26 | 598.94 |                |

| Olap+Beva HRD pos BRCA neg – OS curve |        |        |                |
|---------------------------------------|--------|--------|----------------|
| Fitting                               | AIC    | BIC    | Notes          |
| Weibull                               | 187.07 | 192.22 |                |
| Gompertz                              | 193.48 | 198.63 |                |
| Exp                                   | 194.60 | 197.18 |                |
| LogLog                                | 183.53 | 188.68 |                |
| LogN                                  | 180.04 | 185.19 |                |
| GenGamma                              | 175.94 | 183.66 | Chosen fitting |

| Olap+Beva HRD pos BRCA neg – PFS curve |        |        |                |
|----------------------------------------|--------|--------|----------------|
| Fitting                                | AIC    | BIC    | Notes          |
| Weibull                                | 241.82 | 246.97 |                |
| Gompertz                               | 242.16 | 247.31 |                |
| Exp                                    | 241.05 | 243.62 |                |
| LogLog                                 | 233.11 | 238.25 |                |
| LogN                                   | 228.94 | 234.09 |                |
| GenGamma                               | 221.65 | 229.37 | Chosen fitting |

| Nirap (HRD+, BRCA-) – PFS curve |        |        |                |
|---------------------------------|--------|--------|----------------|
| Fitting                         | AIC    | BIC    | Notes          |
| Weibull                         | 249.06 | 254.17 |                |
| Gompertz                        | 245.56 | 250.67 |                |
| Exp                             | 247.06 | 249.62 |                |
| LogLog                          | 240.86 | 245.97 |                |
| LogN                            | 237.32 | 242.43 |                |
| GenGamma                        | 232.64 | 240.30 | Chosen fitting |

| Nirap (HRD+, BRCA+) – PFS curve |     |     |       |
|---------------------------------|-----|-----|-------|
| Fitting                         | AIC | BIC | Notes |

|          |        |        |                |
|----------|--------|--------|----------------|
| Weibull  | 385.43 | 391.48 |                |
| Gompertz | 384.12 | 390.17 |                |
| Exp      | 384.06 | 387.09 |                |
| LogLog   | 375.76 | 381.81 |                |
| LogN     | 369.81 | 375.86 |                |
| GenGamma | 362.21 | 371.28 | Chosen fitting |

| Nirap (HRD-) – PFS curve |        |        |                |
|--------------------------|--------|--------|----------------|
| Fitting                  | AIC    | BIC    | Notes          |
| Weibull                  | 499.24 | 505.50 |                |
| Gompertz                 | 491.68 | 497.94 |                |
| Exp                      | 497.79 | 500.92 |                |
| LogLog                   | 458.11 | 464.37 |                |
| LogN                     | 456.46 | 462.72 |                |
| GenGamma                 | 436.72 | 446.11 | Chosen fitting |

| Beva (HRD-) – OS curve |        |        |                |
|------------------------|--------|--------|----------------|
| Fitting                | AIC    | BIC    | Notes          |
| Weibull                | 192.74 | 197.62 |                |
| Gompertz               | 199.13 | 204.01 |                |
| Exp                    | 204.04 | 206.48 |                |
| LogLog                 | 189.48 | 194.37 |                |
| LogN                   | 187.78 | 192.67 | Chosen fitting |
| GenGamma               | 189.56 | 196.89 |                |

| Beva (BRCA-) – OS curve |        |        |       |
|-------------------------|--------|--------|-------|
| Fitting                 | AIC    | BIC    | Notes |
| Weibull                 | 499.47 | 506.74 |       |
| Gompertz                | 524.88 | 532.15 |       |
| Exp                     | 600.51 | 604.15 |       |

|          |        |        |                |
|----------|--------|--------|----------------|
| LogLog   | 491.92 | 499.19 |                |
| LogN     | 491.89 | 499.17 | Chosen fitting |
| GenGamma | 493.31 | 504.22 |                |

| <b>Beva (BRCA-) – PFS curve</b> |            |            |                |
|---------------------------------|------------|------------|----------------|
| <b>Fitting</b>                  | <b>AIC</b> | <b>BIC</b> | <b>Notes</b>   |
| Weibull                         | 687.59     | 694.87     |                |
| Gompertz                        | 722.06     | 729.33     |                |
| Exp                             | 722.45     | 726.09     |                |
| LogLog                          | 619.50     | 626.77     | Chosen fitting |
| LogN                            | 630.13     | 637.41     |                |
| GenGamma                        | 629.27     | 640.19     |                |

## References

Diaby V, Adunlin G, Montero AJ. Survival modeling for the estimation of transition probabilities in model-based economic evaluations in the absence of individual patient data: a tutorial. *Pharmacoeconomics*. 2014 Feb;32(2):101-8.

Guyot P, Ades AE, Ouwens MJ, Welton NJ. Enhanced secondary analysis of survival data: reconstructing the data from published Kaplan-Meier survival curves. *BMC Med Res Methodol*. 2012 Feb 1;12:9.

Wei Y, Royston P. Reconstructing time-to-event data from published Kaplan-Meier curves. *Stata J*. 2017 Oct;17(4):786-802.