The complete summary table for the three case studies.

| | **FIRST (Revlimid)** | **INO-VATE (Inotuzumab)** | **GOG-0128 (Bevacizumab)** |
|---|---|---|---|
| **Trial Information** | | | |
| Full name | Frontline Investigation of Revlimid Plus Dexamethasone versus Standard Thalidomide | Inotuzumab Ozogamicin trial to investigate Tolerability and Efficacy | Gynecologic Oncology Group (number 0128) |
| Disease | Transplant-ineligible patients with myeloma | Acute lymphoblastic leukemia | Ovarian cancer |
| Primary endpoint | Progression-free survival with continuous lenalidomide-dexamethasone versus MPT | Overall survival and complete remission (including complete remission with incomplete hematologic recovery) | Cancer PFS:<br>1. An increase in the CA-125 level according to Gynecologic Cancer Intergroup criteria 21;<br>2. Global deterioration of health;<br>3. Death from any cause |
| Therapies | 1. Melphalan + prednisone + thalidomide (MPT)<br>2. Lenalidomide + low-dose dexamethasone for eighteen 28-day cycles (Rd continuous)<br>3. Continued Rd beyond eighteen 28-day cycles (Rd18) | 1. Standard intensive chemotherapy<br>2. Inotuzumab ozogamicin | 1.Carboplatin and paclitaxel (CPP)<br>2. CPP with concurrent bevacizumab and followed by bevacizumab single agent (CPB15+)<br>3. CPP with concurrent bevacizumab (CPB15) |
| Trials information | Multicenter randomized (1:1:1) open-label | Multicenter randomized (1:1) open-label | Multicenter randomized (1:1:1) double-blind |
| Sample size | 1082 | 326 | 1248 |
| Accrual time (months) | 32 | 36 | 24 |
| Follow-up time (months) | 60 | 42 | 42 |
| **Assumption of Proportionality** | | | |

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| | **FIRST (Revlimid)** | **INO-VATE (Inotuzumab)** | **GOG-0128 (Bevacizumab)** |
|---|---|---|---|
| G-T test | $p < 1.0$ e-6 | $p = 5.0$ e-1 | $p = 8.0$ e-4 |
| Schoenfeld's global test | $p < 1.0$ e-7 | $p = 3.5$ e-1 | $p = 1.6$ e-3 |
| Hazard rate plot | Violation | Violation | Violation |
| NPH type | Early crossing / Delayed effect | Delayed effect | Diminishing effect / Late crossing |
| **Methods and Conclusions from the Comparison Paper [5]** | | | |
| Log-rank test (1-sided) | $p < 1.0$ e-4 | $p = 2.0$ e-2 | $p < 1.0$ e-4 |
| Max-Combo test (1-sided) | $p < 1.0$ e-9 (much smaller) | $p = 2.1$ e-3 | $p < 1.0$ e-8 (much smaller) |
| Weight selected | FH (0, 1) | FH (0, 1) | FH (1, 0) |
| Discussion | When there is a delayed treatment effect, the MaxCombo test tends to have a higher power in testing the hypotheses, however, with sufficient follow-up and sample size, the log-rank test may overcome this deficiency | The improvement in power with the MaxCombo test may not be apparent when NPH is marginal | The large sample size in both arms would have provided adequate power |
| **Conclusions from the Original Papers [1, 4, 3, 2]** | | | |

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| | **FIRST (Revlimid)** | **INO-VATE (Inotuzumab)** | **GOG-0128 (Bevacizumab)** |
|---|---|---|---|
| Conclusions | 1.Log-rank test for PFS:<br>Rd continuous vs. MPT (HR=0.72, p <0.001)<br>Rd continuous vs. Rd18 (HR=0.70, p <0.001)<br>Rd18 vs. MPT (HR=1.03, p=0.700)<br>2. OS at 3 years: 70%, 66%, 62% for Rd continuous, Rd18, and MPT;<br>OS at 4 years: 59%, 56%, 51%<br>3. Log-rank test for OS:<br>Rd continuous vs. MPT (HR=0.78, p=0.020) | 1. Median PFS:<br>IO 5mo vs. Standard 1.8mo<br>2. Log-rank test of disease progression:<br>HR=0.45, p <0.001<br>3. Median OS:<br>IO 7.7mo vs. Standard 6.7mo<br>4. Log-rank test of death:<br>HR=0.77, p=0.040<br>5. The rate of 2-year OS:<br>IO 23% vs. Standard 10% | 1. Median PFS:<br>10.3, 11.2, and 14.1 months in the CPP, CPB15, and CPB15+<br>2. Log-rank test of progression or death:<br>CPB15 vs. CPP (HR=0.91, p=0.160)<br>CPB15+ vs. CPP (HR=0.717, p <0.001)<br>3. Median OS:<br>39.3, 38.7, and 39.7 months in the CPP, CPB15, and CPB15+<br>4. LR test of death:<br>CPB15 vs. CPP (HR=1.04, p=0.760)<br>CPB15 vs. CPB15+ (HR=0.92 p=0.450)<br>5. Quality of life:<br>no significant differences across the three treatment groups<br>6. Mean FACT-O TOI scores before cycle 4:<br>CPB15 vs. CPP (-2.70, p <0.001)<br>CPB15+ vs. CPP (-3.00, p <0.001) |

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