















































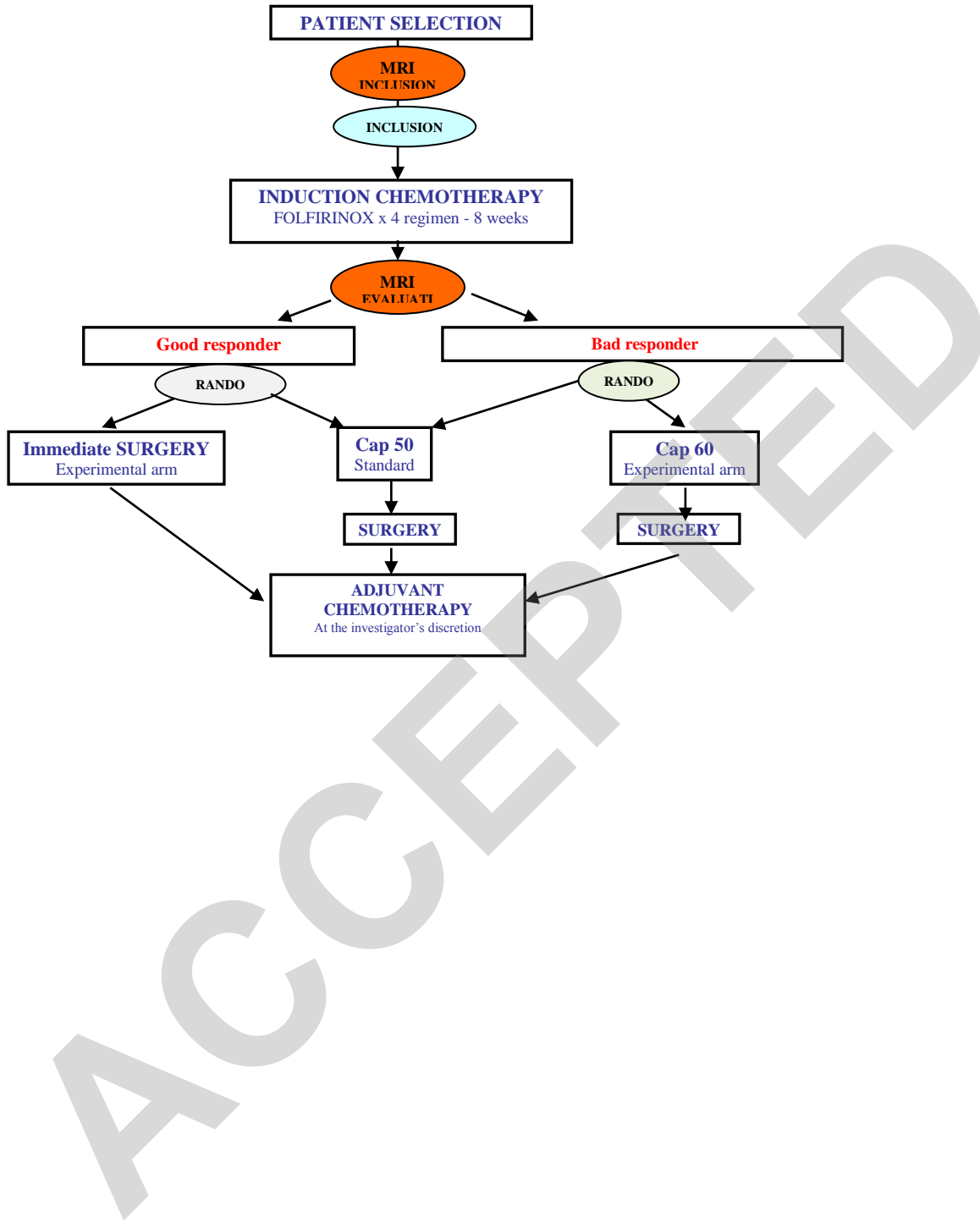
**Table 1.** Patient characteristics at baseline (n=133).

|  | Good responders  |                    | Bad responders    |                  |
|--|------------------|--------------------|-------------------|------------------|
|  | Arm A<br>(n=11)  | Arm B<br>(n=19)    | Arm C<br>(n=52)   | Arm D<br>(n=51)  |
| Sex, n (%)   |                  |                    |                   |                  |
| Male   | 5 (45.5)         | 11 (57.9)          | 34 (65.4)         | 40 (78.4)        |
| Female   | 6 (54.5)         | 8 (42.1)           | 18 (34.6)         | 11 (21.6)        |
| Age (years), median<br>(range)                     | 66.0 (44-78)     | 63.0 (39-75)       | 61 (22-82)        | 62 (22-80)       |
| WHO Performance<br>Status, n (%)                   |                  |                    |                   |                  |
| 0  | 10 (90.9)        | 15 (79.0)          | 40 (76.9)         | 35 (68.6)        |
| 1  | 1 (9.1)          | 4 (21.0)           | 11 (21.2)         | 14 (27.4)        |
| 2  | 0                | 0                  | 1 (1.9)           | 2 (3.9)          |
| BMI, median (range)                                | 25.3 (18.5-33.6) | 24.6 (16.9-32.5)   | 25.4 (16.9-34.0)  | 25.5 (18.3-41.3) |
| Tumor topography, LP-<br>LA (cm), median (range)   | 1.5 (0-5.8) *    | 0 (0-10) *         | 3.3 (0-11) *      | 2.2 (0-44) *     |
| Circumference $\geq$ 50%,<br>n (%)                 | 6 (66.7)         | 6 (50.0)           | 35 (94.6)         | 26 (74.3)        |
| Tumor volume (cm <sup>3</sup> ),<br>median (range) | 23.0 (3.0-148) * | 22.0 (10.0-57.4) * | 43.0 (8.3-387) *  | 47.4 (3.3-312) * |
| CRM (mm), median<br>(range)                        | 0 (0-3)          | 0 (0-5)            | 0 (0-20)          | 0 (0-5)          |
| EMS (mm), median<br>(range)                        | 6.0 (3.0-11.0) * | 4.0 (1.0-16.0) *   | 10.0 (1.5-40.0) * | 12.0 (0.5-50.0)  |

|                |          |           |           |           |
|----------------|----------|-----------|-----------|-----------|
| T stage, n (%) |          |           |           |           |
| T3             | 11 (100) | 19 (100)  | 40 (76.9) | 38 (74.5) |
| T4             | 0        | 0         | 12 (23.1) | 13 (25.5) |
| N stage, n (%) |          |           |           |           |
| N0             | 2 (18.2) | 4 (21.0)  | 2 (3.8)   | 1 (2.0)   |
| N1             | 9 (81.8) | 14 (73.7) | 50 (96.2) | 4 (98.0)  |
| Nx             | 0        | 1 (5.3)   | 0         | 0         |

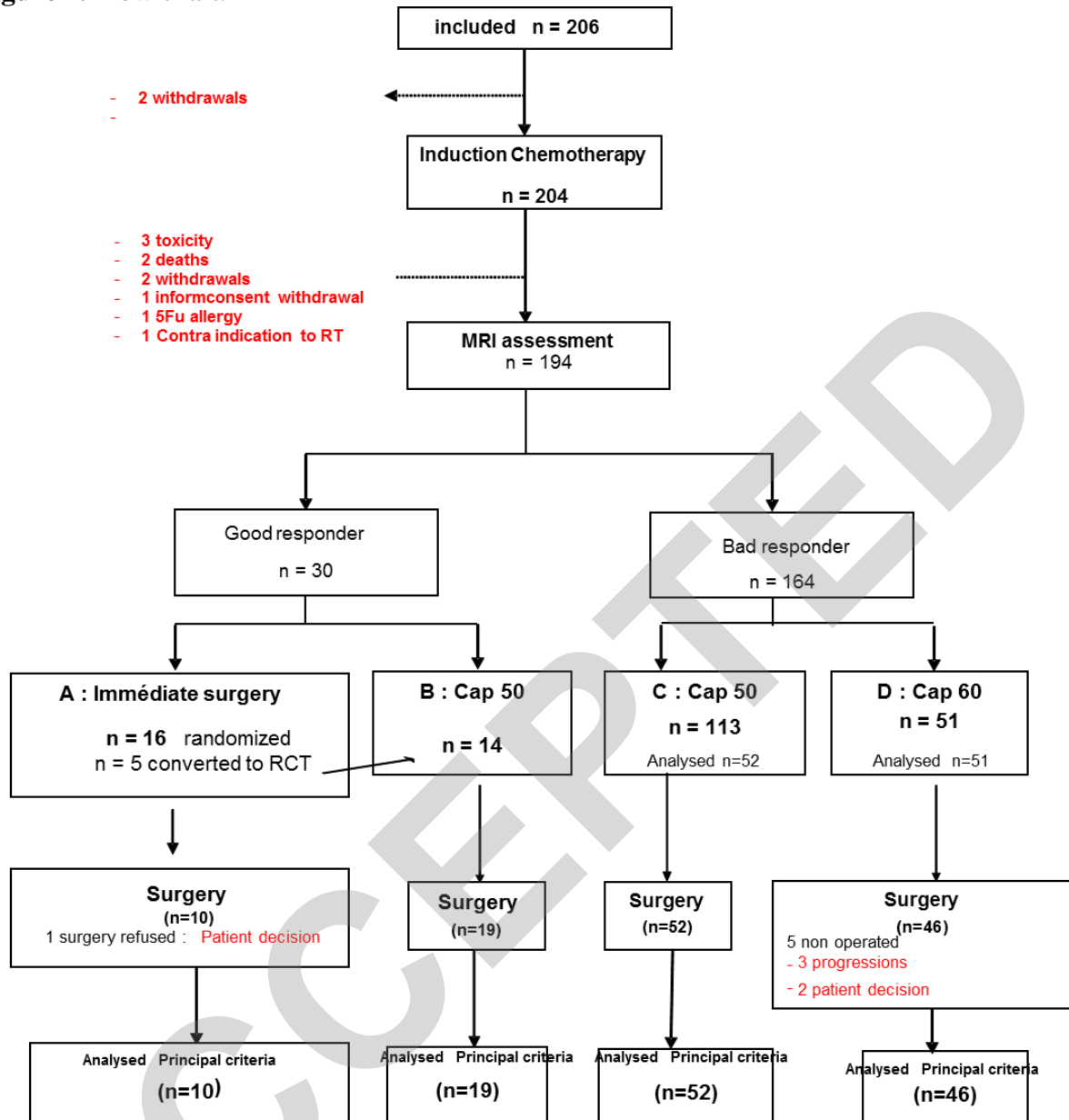
\*(Statistically significant results:  $p < 0.05$ ). Arm A: immediate surgery; arm B: standard radiochemotherapy (Cap 50: 50 Gy irradiation and 1600 mg/m<sup>2</sup> oral capecitabine daily) plus surgery; arm C: Cap 50 before surgery; arm D: intensive radiochemotherapy (Cap 60: 60 Gy irradiation) before surgery. BMI: body mass index; CRM: circumferential resection margin; EMS: extramural spread; LP-LA: lower pole-levator ani; WHO: World Health Organization.

**Figure 1.** Trial design.



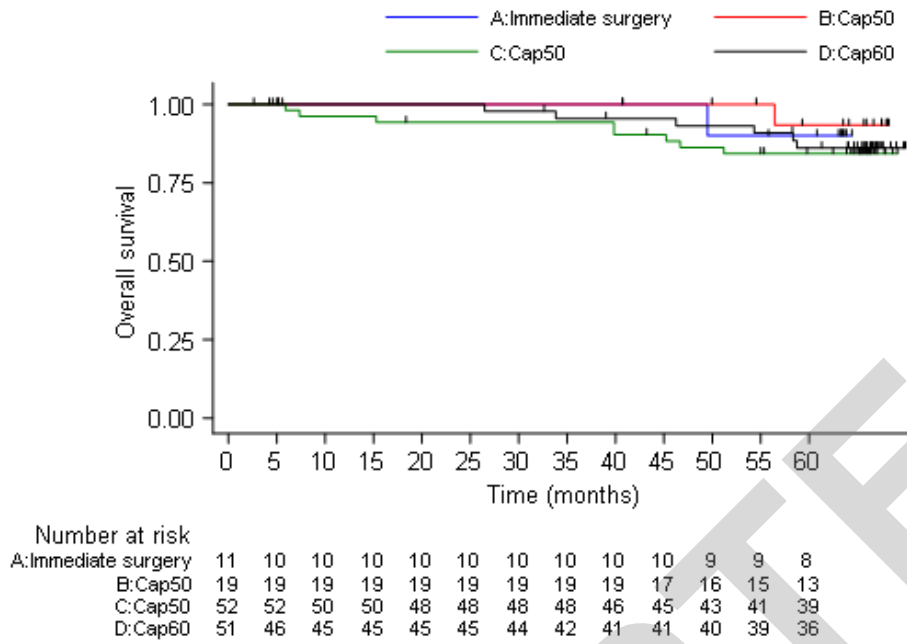


**Figure 2.** Flow chart.

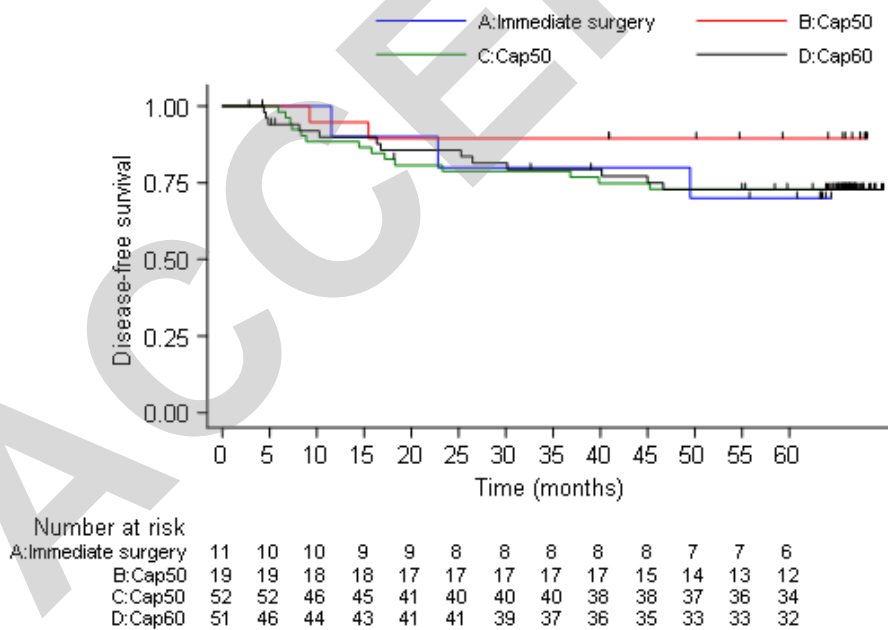


**Figure 3.** 5-year results: a) overall survival; b) disease-free survival; c) metastasis rate.

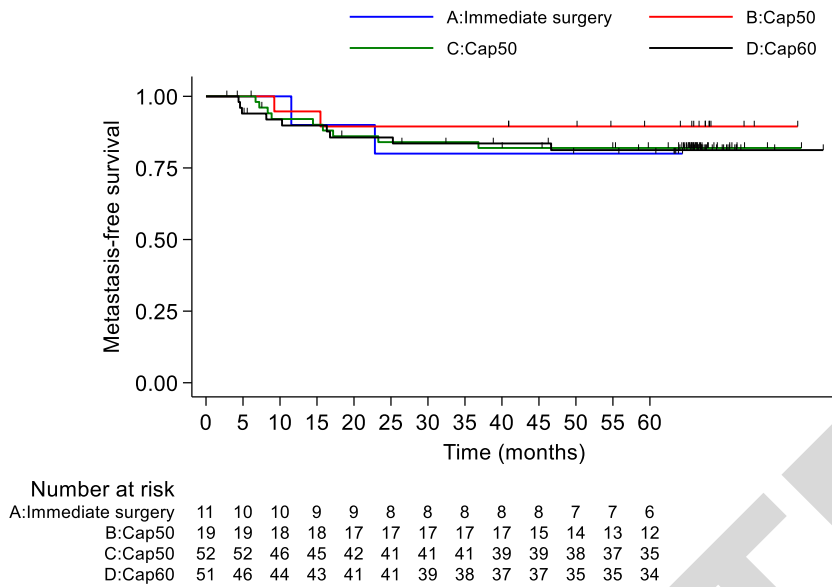
a)



b)

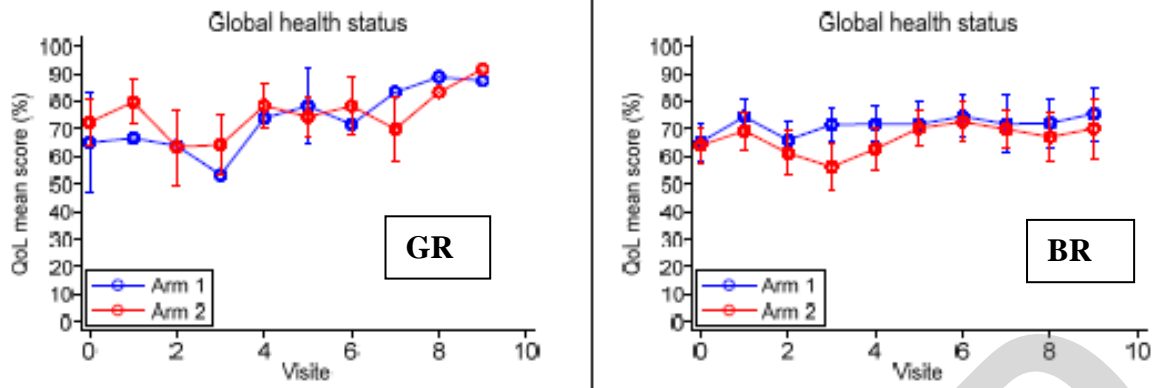


c)



Good responders: Arm A, immediate surgery; arm B, radiochemotherapy (Cap50) before surgery; Bad responders: arm C, radiochemotherapy (Cap50) before surgery; arm D, radiochemotherapy (Cap 60) before surgery.

**Figure 4.** Quality of life: health status.



Left: GR=good responder. Arm A (1), surgery; arm B (2), radiochemotherapy (Cap50: 50 Gy irradiation and 1600 mg/m<sup>2</sup> oral capecitabine daily) + surgery. Right: BR=bad responder. Arm C (2), radiochemotherapy (Cap50) before surgery; arm D (2), radiochemotherapy (Cap 60: 60 Gy irradiation) before surgery.

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