

Doxorubicin and Cyclophosphamide Followed by Docetaxel

Doxorubicin and Cyclophosphamide Followed by Docetaxel ^{2-5,8}																								
Drug	Dose	Route	Administered on day(s)																			Total dose/ cycle		
			1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
Doxorubicin	60 mg/m ²	IV	X																					60 mg/m ²
Cyclophosphamide	600 mg/m ²	IV	X																					600 mg/m ²
Repeated every 21 days for 2 to 4 cycles, followed by:																								
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Docetaxel	100 mg/m ²	IV	X																					100 mg/m ²
Repeated every 21 days for 2 to 4 cycles																								
Alternatives:																								
1. Reverse sequence of D given first for 2 to 4 cycles, followed by AC for 2 to 4 cycles has been used. ^{6,7,9}																								
2. In operable breast cancer, timing of AC followed by D in regard to breast cancer surgery has the following variations:																								
a. AC followed by D as neoadjuvant therapy. ²⁻⁵																								
b. AC as neoadjuvant therapy and D as adjuvant therapy. ⁵																								
c. D as neoadjuvant therapy and AC as adjuvant therapy. ⁶																								

CONSTITUENT DRUGS

- Doxorubicin (*Adriamycin*)
- Cyclophosphamide (*Cytosan*)
- Docetaxel (*Taxotere*)

- AC: > 90% (high) (see p. 520)
- D: 10% to 30% (mild) (see p. 518)

SYNONYMS

- AC followed by D (AC → D)

Hydration

- Cyclophosphamide (see p.521)

USES

- Adjuvant therapy of operable breast cancer¹
- Neoadjuvant therapy of operable breast cancer²⁻⁶
- Treatment of metastatic breast cancer⁷⁻⁹

Hypersensitivity Precaution

- Doxorubicin (see p. 521)
- Docetaxel (see p.521)

SUPPORTIVE CARE

Emetogenicity

- Predicted:

Myeloid Growth Factors

- Prophylactic use not recommended during AC phase but recommended during D phase (see p. 522).
- Febrile neutropenia
 - AC: 2% to 7%^{2-4,6,7,9}
 - D: 1% to 27%^{2,4,6,7,9}
- Neutropenia (grade 3 or 4)

- AC: 14% to 86%^{3,4,6,9}
- D: 20% to 93%^{3,4,6,9}

Extravasation

- Doxorubicin (see p. 522)

Pulmonary

- Docetaxel (see p. 524)

TOXICITIES

Common (> 50%)

- *Dermatologic*
 - Alopecia
 - ◆ Grade 1 or 2: 100% (AC)³; 100% (D)
 - ◆ Grade 3 or 4: 60% to 89% (AC)^{2,4}; 45% to 94% (D)
- *Gastrointestinal*
 - Nausea
 - ◆ Grade 1 or 2: 67% (AC)^{2,3}; 29% (D)³
 - ◆ Grade 3 or 4: 2% to 4% (AC)⁴; 1% to 3% (D)^{2,6,9}
 - Stomatitis
 - ◆ Grade 1 or 2: 67% (AC)³; 66% (D)³
 - ◆ Grade 3 or 4: 1% (AC)^{2,4}; 3% to 8% (D)^{2,4,6,9}
- *Hematologic*
 - Anemia
 - ◆ Grade 1 or 2: 45% (AC)³; 71% (D)³
 - ◆ Grade 3 or 4: 14% (AC)⁶; 2% to 3% (D)^{5,8}
 - Leukopenia
 - ◆ Grade 3 or 4: 4% to 50% (AC)^{4,9}; 10% to 66% (D)^{4,9}
 - Neutropenia
 - ◆ Grade 1 or 2: 29% (AC)³; 11% (D)³
 - ◆ Grade 3 or 4: 14% to 86% (AC)^{3,4,6,7,9}; 20% to 93% (D)^{3,4,6,7,9}
- *Neurologic*
 - Asthenia
 - ◆ Grade 1 or 2: 29% (AC)³; 53% (D)³
 - ◆ Grade 3 or 4: 2% to 7% (AC)^{3,9}; 3% to 9% (D)^{3,6,9}

Frequent (20% to 50%)

- *Cardiovascular*
 - Fluid retention: 5% to 23% (D)^{4,7}
 - Thrombotic events: 20% (D)⁸
- *Gastrointestinal*
 - Diarrhea
 - ◆ Grade 1 or 2: 12% (AC)³; 24% (D)³
 - ◆ Grade 3 or 4: 0.4% (AC)^{2,4,6}; 1% to 7% (D)^{2,4,6,9}
 - Vomiting
 - ◆ Grade 1 or 2: 26% (AC)³
 - ◆ Grade 3 or 4: 2% to 4% (AC)^{2,3,6,9}; 1% to 3% (D)^{2,9}

- *Hematologic*
 - Febrile neutropenia
 - ◆ 2% to 7% (AC)^{2-4,6,7,9}
 - ◆ 1% to 27% (D)^{2,4,6,7,9}
 - *Hypersensitivity*
 - ◆ All grades: 19% to 27% (D)^{7,8}
 - ◆ Grade 1 or 2: 5% (D)³
 - ◆ Grade 3 or 4: 0.3% to 4% (D)^{2,6}
 - *Neurologic*
 - Musculoskeletal pain
 - ◆ All grades: 20% (D)⁸
 - Myalgias
 - ◆ Grade 1 or 2: 24% (D)³
 - Neurosensory toxicity
 - ◆ Grade 1 or 2: 7% (AC)³; 37% (D)³
 - ◆ Grade 3 or 4: 2% (D)⁸
 - *Pulmonary*
 - Dyspnea
 - ◆ Severe: 20% (D)⁸
- ### Infrequent (5% to 19%)
- *Dermatologic*
 - Nail changes
 - ◆ Grade 1 or 2: 2% (AC)³; 13% (D)³
 - ◆ Grade 3 or 4: 0.2% (AC)⁴; 5% (D)⁴
 - Skin changes
 - ◆ Grade 3 or 4: 1% (AC)⁴; 7% (D)⁴
 - *Gastrointestinal*
 - Appetite loss
 - ◆ Grade 3 or 4: 7% (AC)⁴
 - Constipation
 - ◆ Grade 3 or 4: 5% (AC)⁴; 6% (D)⁴
 - Nausea and vomiting: 4% to 13%⁴
 - ◆ Grade 3 or 4: 13% (AC)⁴; 4% (D)⁴
 - *Hematologic*
 - Granulocytopenia
 - ◆ Grade 3 or 4: 6% (AC)²; 2% (D)²
 - Thrombocytopenia
 - ◆ Grade 1 or 2: 10% (AC)³; 3% (D)³
 - ◆ Grade 3 or 4: 1% to 7% (AC)^{4,6}; 1% to 3% (D)^{4,6,9}
 - *Infection*
 - ◆ All grades: 10% (AC)⁷; 15% (D)⁷
 - ◆ Grade 3 or 4: 2% (AC)^{2,4}; 2% to 7% (D)^{2,4,9}
 - *Metabolic*
 - Fatigue
 - ◆ Grade 3 or 4: 10% (AC)⁴; 19% (D)⁴
 - *Neurologic*
 - Neuromotor toxicity
 - ◆ Grade 1 or 2: 2% (AC)³; 5% (D)³
 - ◆ Grade 3 or 4: 0.2% (AC)²; 2% (D)²

Uncommon (1% to 4%)

- **Cardiovascular**
 - Phlebitis or thromboembolism
 - ◆ Grade 3 or 4: 0.5% (AC)²; 1% (D)²
- **Dermatologic**
 - Skin rash
 - ◆ Grade 1 or 2: 3% (D)³
- **Gastrointestinal**
 - Anorexia
 - ◆ Grade 3 or 4: 4% (AC)⁶

RECOMMENDED LABORATORY TESTS

Baseline

- AST/ALT
- Total bilirubin
- Serum creatinine
- CBC with differential

Prior to Each Treatment

- CBC with differential

Recommended Pretreatment Values

- AGC \geq 1,500 cells/mcL²
- ANC \geq 1,500 cells/mcL³
- Platelets \geq 100,000 cells/mcL³
- An ANC of 1,000 cells/mcL and platelets of 75,000 cells/mcL are usually considered acceptable for treatment.

DOSAGE MODIFICATIONS

Renal Function (see p. 526)

Liver Function (see p. 531)

- Docetaxel
 - Reduce dose by 25% for AST 2.5 to 5 times ULN.⁸
 - Omit dose for AST > 5 times ULN.⁸

Myelosuppression

- Febrile neutropenia: Reduce doses of all medications by 25% for febrile neutropenia.^{2,3}
- Neutrophils (AGC or ANC)
 - Hold treatment for up to 1 week for ANC < 1,500 cells/mcL.³
 - Reduce doses of all medications by 17% to 25% for ANC < 500 cells/mcL.⁶⁻⁸
- Platelets
 - Hold treatment for up to 1 week for platelets < 50,000 cells/mcL.³
 - Reduce doses of all medications by 25% for platelets < 25,000 cells/mcL.⁶

Mucositis

- Hold treatment for up to 1 week for grade 2, 3, or 4 mucositis.³

- Reduce doxorubicin and docetaxel doses by 25% for grade 3 or 4 mucositis.⁹

Neurotoxicity

- Reduce doxorubicin and docetaxel doses by 25% for grade 2 neuropathy.⁹
- Discontinue docetaxel for grade 3 or 4 neurotoxicity.^{6,7,9}

Hypersensitivity

- Discontinue docetaxel for grade 3 or 4 hypersensitivity reactions.^{6,8}

Diarrhea

- Reduce docetaxel dose by 25% and doxorubicin and cyclophosphamide doses by 17% for grade 3 or 4 diarrhea.^{7,9}

Edema

- Reduce docetaxel dose by 20% for grade 2 edema.⁸
- Discontinue docetaxel for grade 3 or 4 edema.⁸

Other

- Reduce dose of all medications by 25% for any grade 3 or 4 nonhematologic toxicity.⁶
- Reduce docetaxel dose by 25%, cyclophosphamide dose by 17%, and doxorubicin dose by 17% for grade 3 or 4 nausea or vomiting.⁷
- Discontinue chemotherapy for a greater than 15% decrease in left ventricular ejection fraction to a level below 50%.⁹

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