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Pros and Cons of Monoclonal Antibodies Fixed Dosing Administration in Cancer Patients

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Abstract

Monoclonal antibodies (mAbs) in oncology are usually administered in body-size-based or fixed dosing schedules. However, the minor effects of body size on distribution and elimination of mAbs, as well as a series of practical advantages could support their fixed dosing use.

Abbreviations: FDA: US Food and Drug Administration; EMA: European Medicines Agency; NSCLC: Non Small Cell Lung Cancer; RCC: Renal Cell Carcinoma; BC: Breast Cancer; UC: Urothelial Carcinoma; CHL: Classical Hodgkin's Lymphoma; HNSCC: Head and Neck Squamous Cell Carcinoma; HCC: Hepatocellular Carcinoma; GC: Gastric Cancer; CLL: Cronic Lymphocytic Leukaemia; NHL: Non-Hodgkin's Lymphoma; FL: Follicular Lymphoma; DLBCL: Diffuse Large B-Cell Lymphoma; ; MSI-H: High Microsatellite Instability; IV: Intravenous; SC: SubCutaneous Q2W: Every Two Weeks; Q4W: Every Four Weeks

Monoclonal antibodies (mAbs) in oncology are more frequently administered in body-size-based dosing schedules as cytotoxic anticancer drugs. Simulation studies that compared the performance of body-size-based and fixed dosing of a series of mAbs in terms of pharmacokinetic and/or pharmacodynamic variability demonstrated that the preferable option could be the fixed dosing for some of them, while body-size-based dosing for some others [1,2]. However, since mAbs distribute only in extracellular fluids and blood plasma and considering that the change in volume of distribution as well as the change in blood volume is less than the change in body weight, a body-size-based dosing could result in higher plasma levels in obese patients and lower levels in underweight patients [3]. In addition the mAbs fixed dosing use showed a series of practical advantages such as a decrease of amount of drug wasting or a reduction of errors during drug preparation (Table 1).

Table 1: Pros and Cons of mAbs fixed dosing administration.

Pros	Cons
Reduction of preparation time	Administration of a higher dose than the correspondent personalized dose
Decrease chance of dosing errors	Increase of drug cost (see above)
Reduced amount of drug wasting when pooling of preparation is not possible	
Use of the preparation for other patients when treatment is cancelled at the last minute	
Reduction of inter-subject variability in drug exposure	
*Decrease of infusion time and active healtcare professional time	
Reduction in costs (see above)	

Note: *For subcutaneous formulations.

Table 2: Flat dose of monoclonal antibodies and route of administration.

Name	Approved Flat Dosing		Oncological Indications		Route of Administration
	FDA	EMA	FDA	EMA	
Nivolumab	240 (Q2W) or 480 mg (Q4W)		Melanoma, NSCLC, RCC, UC, cHL, HNSCC, HCC		IV
Pembrolizumab	200mg	200mg	melanoma, NSCLC, UC, cHL, HNSCC, MSI-H, GC	NSCLC, cHL, UC	IV
Pertuzumab	840 (loading dose)/420mg	840 (loading dose)/420mg	HER2+ BC	HER2+ BC	IV
Obinutuzumab	1000mg	1000mg	CLL, FL	CLL, FL	IV
Ofatumumab	300mg (day 1)/ 1000mg	300 mg (day 1)/ 2000mg	CLL	CLL	IV
Rituximab	1400mg or 1600mg	1400mg	FL, DLBCL, CLL	NHL, FL	SC
Trastuzumab	600mg	600mg	HER2+ BC	HER2+ BC	SC

For these reasons several mAbs are actually available on the market for fixed dosing administration by intravenous (IV) or subcutaneous (SC) route (Table 2) [4]. Regarding the impact of the mAbs dosing on the costs there are divergent opinions. For example on one hand, fixed dose can reduce costs especially when pooling in preparation is not possible, on the other hand, as recently reported by Goldstein et al. for pembrolizumab, the prescribed flat dosing could be significantly higher than the correspondent personalized dose with subsequent increase in drug costs [5,6]. In conclusion, both mAbs dosing approaches can be considered in clinical practice; however, in our opinion, given also many practical advantages fixed dosing, if available, should be the preferred choice.

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